

MolDX: Biomarkers in Cardiovascular Risk Assessment

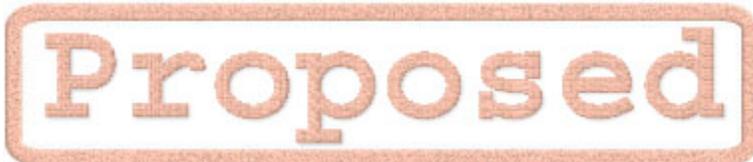
Noridian Healthcare Solutions, LLC



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Title XVIII of the Social Security Act (SSA), §1862(a)(1)(A), states that no Medicare payment shall be made for items or services that “are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.”

Title XVIII of the Social Security Act, §1833(e), prohibits Medicare payment for any claim lacking the necessary documentation to process the claim.

42 Code of Federal Regulations (CFR) §410.32 Diagnostic x-ray tests, diagnostic laboratory tests, and other diagnostic tests: Conditions.

**CMS National
Coverage
Policy**

CMS Internet Online Manual Pub. 100-02 (Medicare Benefit Policy Manual), Chapter 15, Section 80, “Requirements for Diagnostic X-Ray, Diagnostic Laboratory, and Other Diagnostic Tests”

CMS Internet-Only Manuals, Publication 100-04, Medicare Claims Processing Manual, Chapter 16, §50.5 Jurisdiction of Laboratory Claims, 60.12 Independent Laboratory Specimen Drawing, 60.2. Travel Allowance.

CMS Internet Online Manual Pub. 100-04 (Medicare Claims Processing Manual), Chapter 23 (Section 10) “Reporting ICD Diagnosis and Procedure Codes”

Jurisdiction California - Northern

Super MAC J - E

Jurisdiction

Coverage Guidance



Indications and Limitations

This policy pertains to CV risk assessment testing in patients with pre-existing risk factors including but not limited to pre-diabetes or diabetes, smoking, hypertension, or hyperlipidemia. Lipid profile/panel testing (total cholesterol, high density lipoprotein-cholesterol (HDL-C), triglycerides, and low density lipoprotein-cholesterol (LDL-C)) or any one component of the panel is covered according to the indications and limitation of coverage by CMS NCD 190.23, and not further discussed in this policy. This policy does cover hs-CRP in a subset of patients as outlined in the hs-CRP discussion that follows.

However, all non-traditional lipid markers and other non-lipid biomarkers for CV risk assessment are considered investigational and are not covered by Medicare because there is absent or insufficient scientific data to demonstrate a causal relationship, or conflicting data, or no data to demonstrate that testing for any of the following markers improves patient outcomes:

**Coverage
Indications,
Limitations
and/or
Medical
Necessity**

- Lipoprotein subclasses;
- LDL particles;
- Intermediate density lipoproteins;
- High density lipoprotein AI9LpAI and AI/AII;
- Lipoprotein(a);
- Apolipoprotein B (Apo B), apo A-I and apo E;
- Lipoprotein-associated phospholipase A2 (Lp-PLA2)
- BNP
- Cystatin C
- Thrombogenic/hematologic actors
- Interleukin-6 (IL-6), tissue necrosis factor- a (TNF- a) , plasminogen activator inhibitor-1 (PAI-1) and IL-6 promoter polymorphism
- Free fatty acids
- Visfatin, angiotensin-converting enzyme 1 (ACE2) and serum amyloid A
- Microalbumin
- Myeloperoxidase (MPO)
- Homocysteine and methylenetetrahydrofolate reductase (MTHFR) mutation testing
- Uric acid

- Vitamin D
- White blood cell count
- Long-chain omega-3 fatty acids in red blood cell membranes
- Gamma-glutamyltransferase (GGT)
- Genomic profiling including CardiaRisk angiotensin gene
- Leptin, ghrelin, adiponectin and adipokines including retinol binding protein 4 (RBP4) and resistin
- Inflammatory markers including VCAM-1, P-selectin (PSEL) and E-selectin (ESEL)
- Cardiovascular risk panels

Note #1: There is no Medicare benefit for screening CV risk assessment testing for asymptomatic (without signs or symptoms of disease) patients. Screening asymptomatic patients for cardiovascular risk is statutorily excluded by Medicare and will not be addressed in this policy.

Note #2: FDA approval/clearance means that a test/assay has analytical and clinical validity. The FDA does not review clinical utility (that the test/assay demonstrates improved patient outcomes). To meet Medicare's "reasonable and necessary" criteria for coverage, a test/assay must have proven clinical utility.

Traditional vs Non-traditional CV Risk Assessment

During the last two decades the interest in CV biomarkers as early screening tools has risen dramatically, largely fueled by the recognition that traditional CV risk factors (diabetes, smoking, hypertension and hyperlipidemia) do not fully explain individual variation in CV risk, and by advances in genetic and molecular research. Risk assessment for determining the 10-year risk for developing CHD is traditionally carried out using the Framingham risk score (<http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3xsum.pdf>) or other classification that incorporates a lipid profile in the calculation.

Despite the Framingham risk-scoring tool, clinicians have sought non-traditional lipid and other biomarker measurements to predict CV events. The most promising biomarkers are the ones that closely correlate with the pathophysiological process of the disease. In general, there is evidence that some of these biomarkers may alter risk categorization (higher or lower) compared to traditional risk prediction, but it has not been established that changes in categorization provides clinically actionable information beyond that of traditional lipid measures. In addition, no study has provided high-quality evidence that measurement of non-traditional lipid and other biomarkers leads to changes in management that improve health outcomes.

To provide clinically useful knowledge, a biomarker should meet the following criteria:

- Adds clinical knowledge that improves patient outcomes (criteria for Medicare “reasonable and necessary”);
- Provides risk information that is independent of established predictors;
- Is easy to measure and interpret in the clinical setting; and
- Is accurate, reproducible and standardized.

From a purely economic point of view, one would also expect a favorable cost-benefit ratio, although this does not carry significance with Medicare coverage determinations.

High-sensitivity C-reactive protein (hs-CRP)

CRP is a protein produced in the liver during episodes of acute inflammation or infection. The hs-CRP test measures CRP that is in the normal range for healthy people, and is used to distinguish people with low normal levels from those with high normal levels. In recent years, prospective epidemiologic studies have demonstrated that inflammation is essential for CV disease pathogenesis and that high normal levels of hs-CRP correlate with an increased risk of CV events such as myocardial infarction (MI), stroke, sudden cardiac death and peripheral vascular disease (PVD) even when lipid levels are within acceptable ranges. The American Heart Association (AHA) and the US Centers for Disease Control and Prevent (CDC) recommend averaging two hs-CRP levels obtained two weeks apart. Based on hs-CRP test results, they recognize: low (<1.0 mg/L), average (1.0-3.0 mg/L) and high (>3.0 mg/L) risk groups.

In 2009, the US Preventive Services Task Force (USPSTF) report on the use of non-traditional risk factors noted there is insufficient evidence to recommend the use of non-traditional risk factors to screen asymptomatic individuals with no history of CHD to prevent CHD events. The non-traditional risk factors in their recommendation included: hs-CRP, ankle-brachial index (ABI), leukocyte count, fasting blood glucose level, periodontal disease, carotid intima-media thickness, coronary artery calcification (CAC) score on electron beam computerized tomography (EBCT), homocysteine level, and lipoprotein(a) level. The USPSTF stated there is insufficient evidence to determine the percentage of intermediate-risk individuals who would be reclassified by screening with non-traditional risk factors, other than hs-CRP or ABI. For individuals re-classified as high-risk by hs-CRP or ABI, data are not available to determine whether they benefit from additional treatment. They note the potential harms resulting from re-classification including the use of medications without proven benefit and psychological effects. The USPSTF stated that clinicians should continue to use the Framingham model to assess CHD risk and guide risk-based preventive therapy.

While data from the Physicians’ Health Study and Framingham Heart Study

have shown that hs-CRP measurements may result in reclassification of an individual's risk compared to standard risk prediction models, meta-analysis including data from the second Northwick Park Heart Study (NPHS II) and the Edinburgh Artery Study concluded that the ability of hs-CRP to reclassify risk correctly was modest and inconsistent.

The Jupiter trial, a randomized, double-blind, placebo-controlled trial of the use of rosuvastatin vs placebo in the primary prevention of CVD in patients without diabetes with LDL-C <130mg/dL and CRP =2 mg/dL was associated with a significant reduction in the primary endpoint of CV events. These findings suggest that hs-CRP measurement in highly preselected patients may have important clinical implications. However, the Jupiter study was not a trial of hs-CRP because individuals with unknown or low hs-CRP concentrations were not studied. Despite evidence that elevated hs-CRP levels are associated with increased risk of CHD, it has not been determined whether hs-CRP is causally related to CHD.

In 2010, The American College of Cardiology Foundation and the American Heart Association (ACCF/AHA) published guidance as to when and in whom to measure blood levels of hs-CRP. The guidance states that hs-CRP levels may assist in the selection of patients for statin therapy according to the following criteria (Class IIa; Level of evidence (LOE): B):

- Men >50 years of age, or women >60 years of age or older,
- LDL-C <130 mg/dL
- Patients not on lipid-lowering, hormone replacement, or immunosuppressant therapy,
- Patients without clinical CHD, diabetes, chronic kidney disease, severe inflammatory conditions, or contraindications to statins

For example, a patient may appear to have a low or low-moderate elevated risk of CV events based on traditional risk factor scoring with cholesterol levels, weight, level of exercise, smoking history, diabetes and hypertension. However, an elevated hs-CRP level would indicate that the cardiac risk may be substantially greater than traditional risk factors suggest, and that treatment might be considered. For patients who are already known to have high risk, according to current recommendations, hs-CRP levels will not add any substantially new information, since the patient should already be receiving all available therapy including statins to reduce the risk.

The ACCF/AHA recommended measurement of hs-CRP for CV risk assessment in asymptomatic intermediate-risk men 50 years of age or younger, or women 60 years of age or younger (Class IIb; LOE B). Since screening (asymptomatic patient) is statutorily excluded from coverage, hs-CRP testing for these individuals is not a Medicare benefit. They found no benefit for hs-

CRP testing in asymptomatic high-risk adults or men and women below the ages stated above. (Class III; LOE B).

The Canadian Cardiovascular Society guidelines recommend hs-CRP testing in men older than 50 and women older than 60 years of age who are at intermediate risk (10-19%) according to their Framingham risk score and who do not otherwise qualify for lipid-lowering therapy. They also state that subjects who meet Jupiter criteria can be considered for treatment based on the results of that study.

In the National Academy of Clinical Biochemistry's practice guidelines on emerging CV risk factors, only hs-CRP met the stated criteria as a biomarker for risk assessment in primary prevention. They recommended:

- If the 10-year predicted risk, after standard global risk assessment, is <5%, hs-CRP should not be measured.
- If the 10-year risk is 5-10%, it is expected that 10% might be reclassified to a higher risk group with the test.
- If the risk is intermediate (10-20%), and uncertainty remains as to the use of preventive therapies such as statins or aspirin, then hs-CRP measurement might be useful for further stratification into a higher or lower risk category.

The NACB also recommended that:

- Therapies based on hs-CRP should be based on a clinician's clinical judgment because benefits of such treatment are uncertain;
- There is insufficient data that therapeutic monitoring using hs-CRP over time is useful to evaluate effects of treatment in primary prevention;
- The utility of hs-CRP levels to motivate patients to improve lifestyle behaviors has not been demonstrated;
- Evidence is inadequate to support concurrent measurement of other inflammatory markers in addition to hs-CRP for coronary risk assessment.

In 2012, the American Association of Clinical Endocrinologist gave a 2b recommendation for the use of hs-CRP to stratify borderline CV risk in patients with a standard risk assessment, or those with an LDL-C <130 mg/dL. A European consensus guideline (2012) recommended that hs-CRP testing should not be measured in asymptomatic low- and high-risk patients, and gave a weak recommendation to further stratify patient with an intermediate risk of CVD.

The AHA's statement on non-traditional risk factors and biomarkers in CV disease in youth notes "There is currently no clinical role for measuring CRP

routinely in children when assessing or considering therapy for CVD risk factors.” The AHA also state that it is not clear whether high hs-CRP levels during childhood and adolescence lead to an increased risk of CVD in adult life. While lifestyle changes have been shown to decrease hs-CRP in children, and statins reduce CRP in adults, the AHA indicates there is minimal information available on the effect of statins on hs-CRP in children and whether lowering hs-CRP in children mitigates preclinical disease or CVD in adulthood. Similarly, the National Heart, Blood and Lung Institute (NHBLI) guideline on CV risk in children and adolescents found insufficient evidence to recommend hs-CRP testing in these patient groups.

In summary, Noridian will cover hs-CRP when the patient meets the following criteria:

1. Men must be > 50 years of age; women must be > 60 years of age; **and**
2. Patient has intermediate CV risk (10-20% risk of CVD per 10 years using the Framingham point score); **and**
3. Patient has LDL-C between 100-130 mg/dL; **and**
4. Patient has two or more CHD major risk factors, including
 - o Age (Men > 45 years; Women >55 years)
 - o Current cigarette smoking
 - o Family history of premature CHD (CHD in male first degree relative <55; CHD in female first degree relative <65 years of age)
 - o Hypertension (Systolic > 140 mm Hg, or on anti-hypertensive medication)
 - o Low HDL-C (<40 mg/dL)

All other indications for hs-CRP testing, including therapeutic monitoring to evaluate effects of treatment and utility to motivate patient to improve lifestyle behaviors, are investigational and therefore not covered by Medicare.

Lipoprotein subclasses

Lipoprotein subclass determination based on density, electric charge and other physical chemistry aspect of particles such as nuclear magnetic resonance allow more specific characterization of the major subclasses (VLDL, LDL, IDL and HDL). Studies showed that small, dense LDL particles were highly associated with the occurrence of CVD and diabetes.

LDL Particles (LDL-P) (aka LDL or Lipoprotein Particles or Particle Number, LDL or Lipid Subfractionation, Lipid Phenotyping, Nuclear Magnetic Resonance or NMR Profile)

Small dense LDL with elevated triglyceride levels and low HDL-cholesterol

levels constitute the “atherogenic lipoprotein phenotype” form of dyslipidemia that is a feature of type II diabetes and the metabolic syndrome. Measurement of LDL particle density has been proposed as a technique to further risk stratification in patients with elevated LDL levels or for patients with normal LDL levels who have other high risk factors for CAD, or to predict response to a particular therapy.

Although great progress has been made in the development of refined lipoprotein assessment and such measurements have helped in understanding the atherosclerotic process, it is not known whether measurements beyond traditional lipids can identify CV risk subgroups and how treatment would differ based on subgroup classification. Furthermore, it is not known whether this additional information helps the health care provider to identify with greater precision and accuracy the person who will develop clinical or subclinical CVD.

The NACB does not recommend testing as there is insufficient data that measurement of lipoprotein subclasses can identify CV risk subgroups, how treatment would differ based on subgroup classification and whether, over time, measurement is useful to evaluate the effects of treatments. In addition, the 2010 ACCF/AHA guidelines for assessment of lipoprotein, other lipoprotein parameters and modified lipids state that “measurement of lipid parameters, including lipoproteins, apolipoproteins, particle size, and density, beyond standard fasting lipid profile is not recommended for cardiovascular disease risk assessment in asymptomatic adults.”

Intermediate Density Lipoproteins (Remnant Proteins)

Intermediate density lipoproteins (IDLs) have a density that falls between LDLs and VLDLs, and may be referred to as remnant lipoproteins because they vary in size and contain varying proportion of triglycerides and cholesterol. Although there is abundant evidence the remnant lipoproteins are atherogenic, and a risk factor for CAD, there is no evidence how testing improves patient outcomes.

High Density Lipoprotein (HDL) Subclass (Lipoprotein AI 9LpAI) and Lipoprotein AI/AII (LpAI/AII) and/or HDL3 and HDL2

HDL cholesterol (HDL-C) is the risk indicator most often used in associated with CHD risk. HDL subfractions have been used for risk prediction. However data is lacking how the subfractions aid in the diagnosis and management of CHD. Neither the NCEP nor ACCF/AHA guidelines recommend the routine measurement of HDL subspecies in CHD risk assessment.

Lipoprotein(a) (Lp(a))

Lp(a) is a modified form of LDL in which a large glycoprotein, apolipoprotein(a) is bound to apolipoprotein B. It promotes foam cell formation and the deposition of cholesterol in atherosclerotic plaques, and, because it is structurally similar to plasminogen, Lp(a) may contribute to clot formation. However, the complete role of lipoprotein(a) is not fully understood.

There is no standardized scale for measuring Lp(a) because there is no level that is considered “normal”. Because Lp(a) levels are controlled predominantly by genes, cholesterol-lowering drugs have little effect on lowering Lp(a) levels. Elevated Lp(a) is considered an independent risk factor for cardiovascular events, including myocardial infarction, stroke, CVD, vein graft restenosis, and retinal arterial occlusion and may be used to identify individuals who might benefit from more aggressive treatment of other risk factors. However, regardless of the association between Lp(a) and CV disease, there is no data to suggest that more aggressive risk factor modification improves patient health outcomes.

The NACB specifies that Lp(a) screening is not warranted for primary prevention and assessment of cardiovascular risk. They comment that Lp(a) measurement may be done at the physician’s discretion if the risk is intermediate (10%–20%) and uncertainty remains as to the use of preventive therapies such as statins or aspirin (Recommendation – IIB; LOE – C). They further note there is insufficient evidence to support therapeutic monitoring of Lp(a) concentrations for evaluating the effects of treatment. Due to the level of evidence, Noridian will not cover testing for intermediate risk because there is no data to suggest that more aggressive risk factor modification improves patient health outcomes.

Similarly, the 2010 ACCF/AHA guidelines conclude that apolipoproteins is not recommended for CV disease risk assessment in asymptomatic adults. UpToDate notes that Lp(a) is a modest, independent risk factor for CVD, especially MI, but notes there are no clinical trials that have adequately tested the hypothesis that Lp(a) reduction reduces the incidence of first or recurrent CVD events.

Apolipoprotein B (Apo B), Apolipoprotein A-I (Apo AI), and Apolipoprotein E (Apo E)

Apo B is a constituent of LDL particles, and serves as an indirect measurement of the number of LDL particles. Consequently, elevated levels of Apo B suggest increased levels of small dense LDL particles that are thought to be atherogenic.

Apo AI is the major protein constituent of HDL-C. However, its measurement has not been established as a clinically useful test in determining clinical therapy for patients with CAD or dyslipidemia at the current time.

While Apo B and Apo A-I are thought to be the main structural proteins of atherogenic and anti-atherogenic lipoproteins and particles, testing for these compounds has not been validated as a tool for risk assessment. As such, the 2010 ACCF/AHA guidelines indicate that apolipoproteins testing is not recommended for CV risk assessment in asymptomatic adults.

Apo E, the major constituent of VLDL and chylomicrons, acts as the primary binding protein for LDL receptors in the liver and is thought to play a role in lipid metabolism. Although some individuals hypothesize that Apo E genotypes may be useful in the selection of drug therapy, the value of Apo E testing in the diagnosis and management of CHD is insufficient and needs further evaluation.

The National Cholesterol Education Program (NCEP) expert panel concluded that Apo AI is carried in HDL and it is usually low when HDL is reduced. A low Apo AI thus is associated with increased risk of CHD, but not independently of low HDL. Whether it has independent predictive power beyond HDL-C is uncertain and its measurement is not recommended for routine risk assessment in Adult Treatment Panel (ATP III) Guidelines.

Testing for Lipoproteins

Apolipoproteins

Apolipoproteins are measured in routine clinical laboratories with the use of immunonephelometric or immunoturbidimetric assays. ApoB reflects the number of potentially atherogenic lipoprotein particles because each particle of VLDL, IDL, LDL and lipoprotein(a) particle carries on its surface 1 Apo B100 protein. Most of plasma Apo B is found in LDL particles. HDL particles do not carry Apo B. Instead they carry Apo AI, which does not correspond directly to the concentration of HDL particles in a 1-to-1 fashion.

LDL Gradient Gel Electrophoresis (GGE) (used by Berkeley Heart Lab, Berkeley, CA)

GGE is the most commonly used lab technique to measure LDL particle density. It has been promoted as an important criteria of CHD risk, and as a guide to drug and diet therapy in patients with CAD. While the measurement of LDL subclass patterns may be useful in elucidating possible atherogenic dyslipemia in patients without abnormal total cholesterol, HDL, LDL and triglycerides, there is inadequate evidence that LDL sub-classification by GGE improves outcomes in patients with CV disease.

Density Gradient Ultracentrifugation (DGU) (used by Atherotec Inc, Birmingham, AL)

The Vertical Auto Profile (VAP) test measures the relative distribution of cholesterol within various lipoprotein subfractions, quantifying the cholesterol content in the VLDL, IDL, LDL, lipoprotein(a) and HDL subclasses. It includes components (e.g., total cholesterol, direct measured LDL-C, HDL-C and triglycerides), LDL density (i.e. pattern A versus pattern B), IDL, HDL subtypes, VLDL density and Lp(a), and non-lipid CV risk assessment biomarkers including hs-CRP, homocysteine, Lp-PLA2, apo-E genotype, vitamin D, cystatin and NT-proBNP.

Nuclear Magnetic Resonance Spectroscopy

In this method (NMR LipoProfile® is FDA cleared and available from LipoScience Inc, Raleigh, NC) particle concentrations of lipoprotein subfractions of different size are obtained from the measured amplitudes of their lipid methyl group NMR signals. Lipoprotein particle sizes are then derived from the sum of the diameter of each subclass multiplied by its relative mass percentage based on the amplitude of its methyl NMR signal.

Note: FDA clearance does not mean the test has clinical utility.

Ion-Mobility Analysis

This method (available from Quest Diagnostics Inc, Madison, NJ) measures both the size and concentration of lipoprotein particle subclasses on the basis of gas-phase differential electric mobility.

Summary of Lipoprotein Testing

At the current time, none of the above tests for lipoproteins have better predictive strength than total/HDL-C ratio and there has been no clear benefit for measuring particle number in most studies to date. Additional research is needed to establish the utility of following changes in lipoproteins as a therapeutic target and determine if any subgroups of patients benefit. Consequently, lipoprotein testing is considered investigational and not covered.

Lipoprotein-Associated Phospholipase A2 (Lp-PLA2)

Lp-PLA2 is also known as platelet activating factor acetylhydrolase. This enzyme hydrolyzes phospholipids and is primarily associated with LDLs. It has been suggested that this enzyme has a proinflammatory role in the development of atherosclerosis. Studies show that Lp-PLA2 is an independent predictor of CV risk but fail to demonstrate improved health outcomes. To improve outcomes, studies must demonstrate how risk factors improve risk classification and change in physician practice to improve patient outcomes.

The NCEP ATP III panel concluded that routine measurement of inflammatory

markers (including Lp-PLA2) for the purpose of modifying LDL-cholesterol goals in primary prevention is not warranted. In the 2010 ACCF/AHA guidelines for assessment of CV risk, the experts concluded “lipoprotein-associated phospholipase (Lp-PLA2) might be reasonable for cardiovascular risk assessment in intermediate risk asymptomatic adults”. However, at the current time, it is not known whether Lp-PLA2 concentrations are clinically effective for motivating patients, guiding treatment, or improving outcomes.

B-type Natriuretic Peptide (BNP)

BNP and NT-proBNP, hormones produced by cardiocytes in response to hemodynamic stress, have emerged as preferred biomarkers for assessing heart-related stress. These hormones play a role in the acute setting for use in diagnosing decompensated heart failure. There is evidence that these hormones provide prognostic information of mortality and first CV events beyond traditional risk factors. However, there is currently no evidence that treatment or intervention based on the increased risk implied by these biomarkers improves patient outcomes.

Cystatin C

Cystatin C, encoded by the CST3 gene, is a small serine protease inhibitor protein secreted by all functional cells in the body. It is used as a biomarker for renal function, and in CV risk assessment although there is no evidence that this marker improves outcomes when used in clinical care. The NACB guidelines on Biomarkers of Renal Function and Cardiovascular Disease Risk do not recommend testing. The NCEP advocates clinical studies to characterize the utility of these markers in the global assessment of CV disease risk.

Thrombogenic/Hematologic Factors

Hematologic factors including coagulation factors and platelets play a role in acute coronary syndrome although the precise mechanism is not known. That platelets are involved in this process is supported by strong evidence that aspirin and other antiplatelet therapies reduce the risk of myocardial infarction.

Fibrinogen has also been associated with CHD risk. A high fibrinogen level is associated with increased risk for coronary events, independent of cholesterol levels, while a low fibrinogen indicates a reduced risk even with high cholesterol levels. Other hemostatic factors associated with increased coronary risk include, but are not limited to, activated factor VII (aFVII), tissue plasminogen activator (tPA), plasminogen activator inhibitor-1 (PAI-1), von Willebrand factor (wWF), Factor V Leiden (FVL), Factor II (F2), Protein C (PC) and antithrombin III.

In 2009, the NACB guidelines reported there was sufficient data that fibrinogen

is an independent marker of CVD risk. In addition, measurement of fibrinogen was not recommended because they expressed analytical concerns regarding insufficient assay standardization and uncertainty in identifying treatment strategies. Additionally, the NCEP expert panel concluded “ATPIII does not recommend measurement of prothrombotic factors as part of routine assessment of CHD risk”. They indicated that the strength of the association between thrombogenic/hematologic factors and CHD risk has not been defined and recommended clinical trials that target specific prothrombotic factors.

D-dimer is associated with an increased risk of venous and arterial thrombotic events, irrespective of baseline vascular disease, even after adjusting for confounders such as age, smoking and diabetes. In CVD, an increased fibrin turnover represents not only a prothrombotic state, but also is a marker for the severity of atherosclerosis. Although D-dimer is a simple test that is widely available, it remains unclear whether D-dimer plays a causal role in the pathophysiology of CV adverse events, or whether D-dimer is simply a marker of the extent of disease.

Interleukin-6 (IL-6), Tissue Necrosis Factor- a (TNF-a), Plasminogen Activator Inhibitor-1 (PAI-1), and IL-6 Promoter Polymorphism

Adipose tissue is a prominent source of PAI-1. Recent data indicates there is continuous production of large amounts of active PAI-1 in platelets that may contribute to clot stabilization. PAI-1 is the primary physiological inhibitor of plasminogen activation. Increased PAI-1 expression acts as a CV risk factor and plasma levels of PAI-1 strongly correlate with body mass index (BMI). Similar associations have been reported between PAI-1 activity and plasma insulin and triglyceride levels in patients with CAD and diabetes. However, there is no data that PAI-1 testing changes physician management to improve patient outcomes.

IL-6, an inflammatory cytokine, is involved in metabolic regulation of CRP. IL-6 plays an important role in the process of rupture or erosion of atherosclerotic plaques, and its serum levels are elevated during these events. At the current time, there is no consensus on IL-6 assay methods or reference values, and no data that demonstrates IL-6 testing changes physician management to improve patient outcomes.

Early in atherosclerotic plaque formation, leukocytes adhere to and are entrapped in the endothelial wall, a process mediated by inflammatory adhesion molecules such as P-selectin and ICAM-1 that are modulated by TNF-a. However, to date, these biomarkers have not provided additional predictive power above that of traditional lipid markers.

Because a polymorphism in the promoter region of IL-6 (174 bp upstream from the start site) appears to influence the transcription of the IL-6 gene and plasma

levels of IL-6, this functional polymorphism was considered a candidate gene in the development of CV disease. However, multiple studies have produced inconsistent findings. In a large population-based study, no significant relationship between IL-6 promoter polymorphism and risk of CHD was identified. The authors concluded that IL-6-174 promoter polymorphism is not a suitable genetic marker for increased risk of CHD in person aged 55 years or older.

Free Fatty Acids (FFA, Saturated and Unsaturated)

The role of plasma FFA in thrombogenesis in humans is poorly established and no strong direct evidence is available. Increasing plasma FFA concentration is known to induce endothelial activation, increase plasma MPO level and promote a prothrombotic state in non-diabetic healthy subjects. Studies are ongoing to demonstrate the role of FFA in the pathogenesis of atherosclerosis. However, at the current time, there is sparse data on its role in early atherosclerosis and no evidence how testing improves patient outcomes.

Visfatin, Angiotensin-Converting Enzyme 2 (ACE2) and Serum Amyloid A

Visfatin is an active player promoting vascular inflammation and associated with atherosclerosis-related disease. It is involved in cytokine and chemokine secretion, macrophage survival, leukocyte recruitment by endothelial cells, vascular smooth muscle inflammation and plaque destabilization. Although visfatin has emerged as a promising pharmacological target in the context of CV complications, there is no evidence how testing improves patient outcomes.

The renin-angiotensin system (RAS) plays a major role in the pathophysiology of CVD. The enzyme angiotensin-converting enzyme (ACE) converts angiotensin I into the vasoconstrictor, angiotensin II, the main effector of the renin-angiotensin system. It has been suggested that circulating ACE2 may be a marker of CVD with low levels of ACE2 in healthy individuals and increased levels in those with CV risk factors or disease. However, larger clinical studies are needed to clarify the role of ACE2 as a biomarker of CVD, determine the prognostic significance of circulating ACE2 activity and assess whether the measurement of ACE2 will improve CVD risk prediction.

Serum amyloid A (SAA) is a sensitive marker of inflammation and its elevation has been implicated in obesity and in CVD. It is a highly conserved acute-phase protein, stimulated by proinflammatory cytokines such as IL-6, TNF, interferon-gamma and transforming growth factor-beta (TGF-B). SAA is also a kind of apolipoprotein that is involved in cholesterol metabolism. However, there is sparse data on its role in early atherosclerosis and no evidence how testing improves patient outcomes.

Microalbumin

Microalbuminuria is both a renal risk factor and a CV risk factor in patients with diabetes, and particularly a risk marker of CV mortality in the general population. Microalbuminuria also appears to be a sensitive marker for detecting new onset of hypertension and diabetes. However, for albuminuria to be a target for therapy, one needs to prove that lowering of albuminuria per se is cardioprotective. Albuminuria-lowering effect of antihypertensive agents, particularly those that interfere with RAS, and the use of statins and glycosaminoglycans have been proved in randomized, controlled trial to be cardioprotective. However, few have been directed at albuminuria lowering per se to evaluate the effect on CV outcome. The question remains as to whether microalbuminuria is the consequence or the cause of organ damage, particularly whether high levels of albuminuria in young children reflect normal physiological variations in endothelial function associated with CV and renal risk in later age. While albumin excretion levels may represent a primary marker for success of intervention strategies aimed at repairing vascular function, there is no data how testing improves patient outcomes at the current time.

Myeloperoxidase (MPO)

Elevated levels of myeloperoxidase, secreted during acute inflammation, are thought by some to be associated with coronary disease and predictive of acute coronary syndrome in patients with chest pain. Many studies have implicated MPO in the pathogenesis of atherosclerosis, showing that it is enriched within atheromatous plaques. Inflammatory cells recruited into the vascular wall release MPO-derived reactive oxygen species that can promote endothelial dysfunction by reducing the bioavailability of nitric oxide, generate atherogenic oxidized-LDL, and modify HDL, impairing its function in cholesterol efflux. However, at the current time there is insufficient data to demonstrate that plasma MPO can predict CHD independent of other CVD risk factors and there is no data that demonstrates how plasma MPO levels affect management of individuals at risk for or patients with CHD.

Peroxisome Proliferator Activated Receptors (PPAR) are a key regulator of fatty acid metabolism, promoting its storage in adipose tissue and reducing circulating levels of free fatty acids. Activation of PPAR has favorable effects on surrogate measures of adipocyte function, insulin sensitivity, lipoprotein metabolism, and vascular structure and function. However clinical trials of thiazolidinedione PPAR activators have not provided conclusive evidence that they reduce CV morbidity and mortality.

At the current time, there is no clinical data that demonstrates the clinical utility of testing for lipid peroxidation, isoprostanes, malondialdehyde, nitrotyrosine, S-glutathionylation, oxidized LDL, or oxidized phospholipids. Additionally, genetic testing for genes that regulate cellular and systemic oxidative stress,

including but not limited to, nuclear factor-2 (Nrf-2), peroxisome proliferator-activated receptor gamma-co-activator 1alpha (PCG-1a), and the thioredoxin family or proteins have no clinical data that demonstrates utility.

Homocysteine and Methylenetetrahydrofolate Reductase (MTHFR) Mutation Testing

Homocysteine is an amino acid found in the blood. Observational evidence generally supports the association of homocysteine levels with CV risk, particularly observational data that patients with hereditary homocystinuria, an inborn error of metabolism associated with high plasma levels of homocysteine, have markedly increased risk of CV disease. Folic acid and the B vitamins are involved in the metabolism of homocysteine. Several studies found the higher levels of B vitamins are associated with lower homocysteine levels, while other evidence shows that low levels of folic acid are linked to a higher risk of CHD and stroke. However, large randomized controlled trials do not support a protective effect of folic acid supplementation (rectifying homocysteine levels) in cardiovascular disease.

MTHFR is a key enzyme in folate metabolism. Two variants of the MTHFR polymorphisms result in reduced enzyme activity, impaired methylation and increased risk of CVD, stroke, and hypertension. MTHFR mutation testing has been advocated to evaluate the cause of elevated homocysteine levels.

However, in 2009, the US Preventive Services Task Force (USPSTF) concluded that the evidence was insufficient to assess the benefits and harms of using non-traditional risk factors to screen asymptomatic adults with no history of CHD to prevent CHD events. Homocysteine was one of the non-traditional factors considered in the recommendation. In 2010, later updated in March 2014, the AHA stated that a causal link between homocysteine levels and atherosclerosis has not been established, and noted that high homocysteine levels is not a major risk factor for CV disease. The 2012 American Association of Clinical Endocrinologists (AACE) guidelines for management of dyslipidemia and prevention of atherosclerosis stated that testing for homocysteine, uric acid, PAI-1 or other inflammatory markers is not recommended.

Uric acid

A recent systemic review and meta-analysis suggests that elevated uric acid levels may modestly increase the risk of stroke and mortality. However, future studies are needed to determine whether lowering uric acid levels has any beneficial effects on stroke risk. Data is inadequate to show that uric acid testing changes physician management to improve patient outcomes.

Vitamin D

Low levels of vitamin D are an independent risk factor for CV death in populations without pre-existing CV disease. However, systematic reviews on interventional vitamin D supplementation and CV disease risk reported that vitamin D supplementation had no effect on cardiovascular disease risk, indicating a lack of a causal relationship.

An additional concern regarding vitamin D testing is the considerable variation between results obtained with the various methods (competitive immunoassays, direct detection by high performance liquid chromatography or liquid chromatography combined with tandem mass spectrometry), as well as between laboratories. Immunoassay technologies are less sensitive and specific for vitamin D than liquid chromatography with or without mass spectrometry.

WBC

A large body of data from prospective studies has established an association of leukocyte count with increased risk for CVD events. Leukocytes are thought to play a role in the development and/or progression of atherosclerotic plaques and their rupture due to their proteolytic capacity and oxidative properties. WBC count is correlated with other coronary disease risk factors, including cigarette smoking, BMI, cholesterol level, HDL-C (inversely), triglycerides, diabetes and blood glucose level, physical activity (inversely) and blood pressure. However, the NACB does not recommend WBC testing because clinical utility in reclassifying risk level and identifying treatment strategies is not known.

Long-chain Omega-3 Fatty Acids in Red Blood Cell (RBC) Membranes

It has been proposed that the fatty acid composition of RBCs are an index of long-term intake of eicosapentaenoic (EPA) plus docosahexaenoic (DHA) acids. The omega-3 fatty acids are considered a new modifiable and clinically relevant risk factor for death from CHD. Most studies to date have focused on the association between fish consumption and risk of CHD. In the Rotterdam Study, analysis of EPA plus DHA and fish intake was assessed in relation of incident heart failure (HF). With nearly 5300 study individuals, the authors concluded that their findings did not support a major role for fish intake in the prevention of HF. Not only is there no association between fish intake and EPA+DHA levels regarding prevention of HF, there is no scientific evidence regarding how measurements of RBC omega-3 fatty acids composition would affect management of individuals at risk for or patients with CHD. A recent article (Marai, 2014) notes that the available data do not support testing for omega-3 polyunsaturated fatty acids (EPA + DHA) among healthy subjects and patients with specific cardiac diseases.

Gamma-glutamyltransferase (GGT)

GGT, a marker of excessive alcohol consumption or liver disturbance, is an enzyme catalyzing the first step in extracellular degradation of the anti-oxidant glutathione and is thought to play a role in the atherosclerotic process. Coverage for GGT is limited to the indications and limitations specified in CMS NCD 190.32. Whether serum levels of GGT can aid in the detection of individuals at high risk for incident CV events is under investigation. Despite its potential role in stratifying patient risk, there is no evidence testing improves patient outcomes.

Gene Mutations (any methodology) and Genomic Profiling

Proponents of molecular CV profile testing argue that improvement in CVD risk classification leading to management changes that improve outcomes warrants coverage of these tests. However, the Evaluation of Genomic Applications in Practice and Prevention Working Group (EWG) found insufficient evidence to recommend testing for 9p21 genetic variant or 57 other variants in 28 genes to assess risk for CVD in the general population, specifically heart disease and stroke.

The following genes were included in the EWG's assessment: ACE, AGT, AGTR1, APOB, APOC3, APOE, CBS, CETP, CYBA, CYP11B2, F2, F5, GNB3, GPX1, IL1B, LPL, ITGB3, MTHFR, MTR, MTRR, NOS3, PAI-1, PON1, SELE, SOD2, SOD3, TNF, and 9p21. The EWG found that the magnitude of net health benefit from the use of any of these tests alone or in combination is negligible.

CardiaRisk™ (Myriad, Salt Lake UT) markets a genetic test to identify a mutation in the AGT genes. This test supposedly identifies specific hypertensive patients at increased risk of CV disease and identifies patients likely to respond to antihypertensive drug therapy. However, at the present time there is no literature that points to clinical utility for this test.

Leptin, Ghrelin, Adiponectin, and Adipokines including Retinol Binding Protein 4 (RBP4) and Resistin

Leptin, a satiety factor secreted by adipocytes that is instrumental in appetite regulation and metabolism, is elevated in heart disease. In a recent study, leptin levels and proinflammatory high-density lipoprotein (piHDL) when combined into a risk score (PREDICTS) confers 28-fold increased odds of the presence of any current, progressive, or acquired carotid plaque and significantly associated with higher rates of intima-media thickness. However, there is no data that demonstrates how measurement of leptin levels affects management of individuals at risk for or patients with CHD.

Ghrelin is a hormone produced in the stomach and pancreas that plays a role in hunger and weight gain. In a recent study, ghrelin when incorporated in the CV

risk model improved the prediction of CVD events in hypertensive patients with reclassification of roughly 21%. However, there is no evidence how testing improves patient outcomes.

Adiponectin is an adipose-specific hormone that has anti-inflammatory properties, and is protective against obesity. Particularly in children, measurement of total adiponectin or high-molecular-weight adiponectin (HMW adiponectin) as a biomarker for insulin sensitivity and/or as a risk factor for CVD is gaining support. However, the additive value of adiponectin levels remains unclear and how it changes patient outcomes is not known. It is not recommended clinically in children or adults.

RBP4 is gaining recognition as an adipokine that may play an important role in obesity and insulin resistance. The relationship between RBP4 and other traditional and non-traditional risk factors for CVD, such as inflammatory factors and/or oxidative stress, have not been confirmed in larger populations, and causality has not been established.

Resistin is an adipokine expressed highly in visceral compared with subcutaneous adipose tissue. In the Study of Inherited Risk of Coronary Atherosclerosis (Reilly, 2003), resistin levels were positively correlated with higher coronary calcium scores and correlated with higher levels of soluble TNF- α , receptor-2, Lp(a), and IL-6. The resistin gene (RETN) polymorphism (bp -420 and +299) leads to increased concentrations of the resistin peptide in circulation, which is associated with cardiomyopathy and CAD. One study suggests that in addition to primary risk factors (total cholesterol, LDL, triglycerides and low concentrations of HDL), resistin cytokine may be a risk factor for CVD. However, there is no clinical role for measuring resistin as no data demonstrates how measurement of resistin levels affects management of individuals at risk for or patients with CHD.

Inflammatory Markers – VCAM-1, ICAM-1, P-selectin (PSEL) and E-selectin (ESEL)

Clinical studies have shown that elevated serum concentrations of cell adhesion molecules such as inter-cellular adhesion molecule-1 (ICAM-1), vascular adhesion molecule-1 (VCAM-1), E-selectin (ESEL) and P-selectin (PSEL) may contribute to CVD through their inflammatory effects on the vascular endothelium and be independent risk factors for atherosclerosis and cardiovascular disease (CVD). However, at the current time, testing for these inflammatory markers has not been confirmed in larger populations, causality has not been established and testing has not resulted in improved patient outcomes.

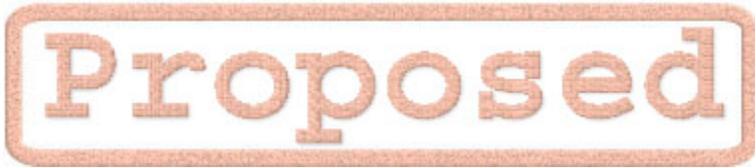
Cardiovascular Risk Panels

Numerous CV risk panels are commercially available. These panels report results for multiple individual CV risk markers and have wide variability in the risk factors included in the panel including different combinations of lipids, non-cardiac biomarkers, measures of inflammation, metabolic and hematologic markers, and/or genetic markers. While the individual risk factors included in CV risk panels have, in most cases been associated with increased risk of CV disease, it is not clear how the results of individual risk factors impact management changes, so it is also not certain how the panels will impact management decisions. The lack of evidence for clinical utility of any individual non-traditional risk factor beyond simple lipid measures predict the lack of evidence for clinical utility for the use of CV risk panels, as there is no evidence that any panel improves patient outcomes. As a result, the use of cardiac risk panels for predicting risk of CV disease is considered not medically reasonable and necessary and therefore, not payable by Medicare.

Some examples of commercially available CV risk panels include, but are not limited to, the following:

- Health Diagnostics Cardiac Risk Panel
- Boston Heart Advanced Risk Markers Panel
- Genova Diagnostics CV Health Plus Genomics Panel
- Metamatrix Cardiovascular Health Profile
- Cleveland HeartLab CVD Inflammatory Panel
- Applied Genetics Cardiac Panel
- Genetiks Genetic Diagnostic and Research Center Cardiovascular Risk Panel

Proposed Process Information



**Associated
Information**

Documentation Requirements

The patient's medical record must contain documentation that fully supports the medical necessity for services included within this LCD. (See "Coverage Indications, Limitations, and/or Medical Necessity") This documentation includes, but is not limited to, relevant medical history, physical examination, and results of pertinent diagnostic tests or procedures.

Documentation supporting the medical necessity should be legible, maintained in the patient's medical record, and must be made available to the MAC upon request.

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**Sources of
Information
and
Basis for
Decision**

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Open Meetings	Meeting Date	Meeting Information	State
	10/01/2015	Embassy Suites - Las Vegas Flamingo Ballroom 4315	American Samoa, California - Entire State, Guam, Hawaii, Nevada,

Swenson Street Las Vegas, Northern Mariana Islands, California -
 NV 89119 Northern, California - Southern

	Meeting Date	Meeting Information	State
Part B MAC Contractor Advisory Committee (CAC) Meetings	10/22/2015	Clark County Medical Association/NV State Medical Association 2590 E Russell Rd Las Vegas, NV 89120	Nevada
	10/09/2015	The Pacific Club, Card Room 1451 Queen Emma St Honolulu, HI 96813	American Samoa, Guam, Hawaii, Northern Mariana Islands
	10/21/2015	DoubleTree by Hilton San Francisco Airport Tiburon/Sausalito Room 835 Airport Boulevard Burlingame, CA 94010	California - Entire State, California - Northern, California - Southern

Comment Period 10/01/2015
Start Date
Comment Period 12/07/2015
End Date
Released to Final Not yet released.

LCD Date
Reason for Proposed LCD Creation of Uniform LCDs...
 Creation of Uniform LCDs With Other MAC Jurisdiction

Proposed LCD Noridian Healthcare Solutions, LLC JE Part B Contractor Medical Director(s)
 Attention: Draft LCD Comments
 PO Box 6783
Contact Fargo, North Dakota 58108-6783
policyb.drafts@noridian.com

Coding Information



Bill Type Codes 999x Not Applicable

Revenue Codes

CPT/HCPCS Codes **Group 1: Paragraph** The following CPT code is covered:
Group 1: Codes
 86141 C-REACTIVE PROTEIN; HIGH SENSITIVITY (HSCR)

Group 2: Paragraph

The following CPT codes are not covered:

84999 is used for Lipoprotein, direct measurement, intermediate density lipoproteins (IDL) (remnant lipoproteins) and is not covered.

Group 2: Codes

81200	ASPA (ASPARTOACYLASE) (EG, CANAVAN DISEASE) GENE ANALYSIS, COMMON VARIANTS (EG, E285A, Y231X)
81201	APC (ADENOMATOUS POLYPOSIS COLI) (EG, FAMILIAL ADENOMATOSIS POLYPOSIS [FAP], ATTENUATED FAP) GENE ANALYSIS; FULL GENE SEQUENCE
81202	APC (ADENOMATOUS POLYPOSIS COLI) (EG, FAMILIAL ADENOMATOSIS POLYPOSIS [FAP], ATTENUATED FAP) GENE ANALYSIS; KNOWN FAMILIAL VARIANTS
81203	APC (ADENOMATOUS POLYPOSIS COLI) (EG, FAMILIAL ADENOMATOSIS POLYPOSIS [FAP], ATTENUATED FAP) GENE ANALYSIS; DUPLICATION/DELETION VARIANTS
81205	BCKDHB (BRANCHED-CHAIN KETO ACID DEHYDROGENASE E1, BETA POLYPEPTIDE) (EG, MAPLE SYRUP URINE DISEASE) GENE ANALYSIS, COMMON VARIANTS (EG, R183P, G278S, E422X)
81206	BCR/ABL1 (T(9;22)) (EG, CHRONIC MYELOGENOUS LEUKEMIA) TRANSLOCATION ANALYSIS; MAJOR BREAKPOINT, QUALITATIVE OR QUANTITATIVE
81207	BCR/ABL1 (T(9;22)) (EG, CHRONIC MYELOGENOUS LEUKEMIA) TRANSLOCATION ANALYSIS; MINOR BREAKPOINT, QUALITATIVE OR QUANTITATIVE
81208	BCR/ABL1 (T(9;22)) (EG, CHRONIC MYELOGENOUS LEUKEMIA) TRANSLOCATION ANALYSIS; OTHER BREAKPOINT, QUALITATIVE OR QUANTITATIVE
81209	BLM (BLOOM SYNDROME, RECQ HELICASE-LIKE) (EG, BLOOM SYNDROME) GENE ANALYSIS, 2281DEL6INS7 VARIANT
81210	BRAF (V-RAF MURINE SARCOMA VIRAL ONCOGENE HOMOLOG B1) (EG, COLON CANCER), GENE ANALYSIS, V600E VARIANT
81211	BRCA1, BRCA2 (BREAST CANCER 1 AND 2) (EG, HEREDITARY BREAST AND OVARIAN CANCER) GENE ANALYSIS; FULL SEQUENCE ANALYSIS AND COMMON DUPLICATION/DELETION VARIANTS IN

- BRCA1 (IE, EXON 13 DEL 3.835KB, EXON 13 DUP 6KB, EXON 14-20 DEL 26KB, EXON 22 DEL 510BP, EXON 8-9 DEL 7.1KB)
- 81212 BRCA1, BRCA2 (BREAST CANCER 1 AND 2) (EG, HEREDITARY BREAST AND OVARIAN CANCER) GENE ANALYSIS; 185DELAGE, 5385INSC, 6174DELT VARIANTS
- 81213 BRCA1, BRCA2 (BREAST CANCER 1 AND 2) (EG, HEREDITARY BREAST AND OVARIAN CANCER) GENE ANALYSIS; UNCOMMON DUPLICATION/DELETION VARIANTS
- 81214 BRCA1 (BREAST CANCER 1) (EG, HEREDITARY BREAST AND OVARIAN CANCER) GENE ANALYSIS; FULL SEQUENCE ANALYSIS AND COMMON DUPLICATION/DELETION VARIANTS (IE, EXON 13 DEL 3.835KB, EXON 13 DUP 6KB, EXON 14-20 DEL 26KB, EXON 22 DEL 510BP, EXON 8-9 DEL 7.1KB)
- 81215 BRCA1 (BREAST CANCER 1) (EG, HEREDITARY BREAST AND OVARIAN CANCER) GENE ANALYSIS; KNOWN FAMILIAL VARIANT
- 81216 BRCA2 (BREAST CANCER 2) (EG, HEREDITARY BREAST AND OVARIAN CANCER) GENE ANALYSIS; FULL SEQUENCE ANALYSIS
- 81217 BRCA2 (BREAST CANCER 2) (EG, HEREDITARY BREAST AND OVARIAN CANCER) GENE ANALYSIS; KNOWN FAMILIAL VARIANT
- 81220 CFTR (CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR) (EG, CYSTIC FIBROSIS) GENE ANALYSIS; COMMON VARIANTS (EG, ACMG/ACOG GUIDELINES)
- 81221 CFTR (CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR) (EG, CYSTIC FIBROSIS) GENE ANALYSIS; KNOWN FAMILIAL VARIANTS
- 81222 CFTR (CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR) (EG, CYSTIC FIBROSIS) GENE ANALYSIS; DUPLICATION/DELETION VARIANTS
- 81223 CFTR (CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR) (EG, CYSTIC FIBROSIS) GENE ANALYSIS; FULL GENE SEQUENCE
- 81224 CFTR (CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR) (EG, CYSTIC

- FIBROSIS) GENE ANALYSIS; INTRON 8 POLY-T ANALYSIS (EG, MALE INFERTILITY)
- 81225 CYP2C19 (CYTOCHROME P450, FAMILY 2, SUBFAMILY C, POLYPEPTIDE 19) (EG, DRUG METABOLISM), GENE ANALYSIS, COMMON VARIANTS (EG, *2, *3, *4, *8, *17)
- 81226 CYP2D6 (CYTOCHROME P450, FAMILY 2, SUBFAMILY D, POLYPEPTIDE 6) (EG, DRUG METABOLISM), GENE ANALYSIS, COMMON VARIANTS (EG, *2, *3, *4, *5, *6, *9, *10, *17, *19, *29, *35, *41, *1XN, *2XN, *4XN)
- 81227 CYP2C9 (CYTOCHROME P450, FAMILY 2, SUBFAMILY C, POLYPEPTIDE 9) (EG, DRUG METABOLISM), GENE ANALYSIS, COMMON VARIANTS (EG, *2, *3, *5, *6)
- 81228 CYTOGENOMIC CONSTITUTIONAL (GENOME-WIDE) MICROARRAY ANALYSIS; INTERROGATION OF GENOMIC REGIONS FOR COPY NUMBER VARIANTS (EG, BACTERIAL ARTIFICIAL CHROMOSOME [BAC] OR OLIGO-BASED COMPARATIVE GENOMIC HYBRIDIZATION [CGH] MICROARRAY ANALYSIS)
- 81229 CYTOGENOMIC CONSTITUTIONAL (GENOME-WIDE) MICROARRAY ANALYSIS; INTERROGATION OF GENOMIC REGIONS FOR COPY NUMBER AND SINGLE NUCLEOTIDE POLYMORPHISM (SNP) VARIANTS FOR CHROMOSOMAL ABNORMALITIES
- 81235 EGFR (EPIDERMAL GROWTH FACTOR RECEPTOR) (EG, NON-SMALL CELL LUNG CANCER) GENE ANALYSIS, COMMON VARIANTS (EG, EXON 19 LREA DELETION, L858R, T790M, G719A, G719S, L861Q)
- 81240 F2 (PROTHROMBIN, COAGULATION FACTOR II) (EG, HEREDITARY HYPERCOAGULABILITY) GENE ANALYSIS, 20210G>A VARIANT
- 81241 F5 (COAGULATION FACTOR V) (EG, HEREDITARY HYPERCOAGULABILITY) GENE ANALYSIS, LEIDEN VARIANT
- 81242 FANCC (FANCONI ANEMIA, COMPLEMENTATION GROUP C) (EG, FANCONI ANEMIA, TYPE C) GENE ANALYSIS, COMMON VARIANT (EG, IVS4+4A>T)
- 81243 FMR1 (FRAGILE X MENTAL RETARDATION 1) (EG, FRAGILE X MENTAL RETARDATION) GENE

- ANALYSIS; EVALUATION TO DETECT ABNORMAL (EG, EXPANDED) ALLELES
- 81244 FMR1 (FRAGILE X MENTAL RETARDATION 1) (EG, FRAGILE X MENTAL RETARDATION) GENE ANALYSIS; CHARACTERIZATION OF ALLELES (EG, EXPANDED SIZE AND METHYLATION STATUS)
- 81245 FLT3 (FMS-RELATED TYROSINE KINASE 3) (EG, ACUTE MYELOID LEUKEMIA), GENE ANALYSIS; INTERNAL TANDEM DUPLICATION (ITD) VARIANTS (IE, EXONS 14, 15)
- 81246 FLT3 (FMS-RELATED TYROSINE KINASE 3) (EG, ACUTE MYELOID LEUKEMIA), GENE ANALYSIS; TYROSINE KINASE DOMAIN (TKD) VARIANTS (EG, D835, I836)
- 81250 G6PC (GLUCOSE-6-PHOSPHATASE, CATALYTIC SUBUNIT) (EG, GLYCOGEN STORAGE DISEASE, TYPE 1A, VON GIERKE DISEASE) GENE ANALYSIS, COMMON VARIANTS (EG, R83C, Q347X)
- 81251 GBA (GLUCOSIDASE, BETA, ACID) (EG, GAUCHER DISEASE) GENE ANALYSIS, COMMON VARIANTS (EG, N370S, 84GG, L444P, IVS2+1G>A)
- 81252 GJB2 (GAP JUNCTION PROTEIN, BETA 2, 26KDA, CONNEXIN 26) (EG, NONSYNDROMIC HEARING LOSS) GENE ANALYSIS; FULL GENE SEQUENCE
- 81253 GJB2 (GAP JUNCTION PROTEIN, BETA 2, 26KDA, CONNEXIN 26) (EG, NONSYNDROMIC HEARING LOSS) GENE ANALYSIS; KNOWN FAMILIAL VARIANTS
- 81254 GJB6 (GAP JUNCTION PROTEIN, BETA 6, 30KDA, CONNEXIN 30) (EG, NONSYNDROMIC HEARING LOSS) GENE ANALYSIS, COMMON VARIANTS (EG, 309KB [DEL(GJB6-D13S1830)] AND 232KB [DEL(GJB6-D13S1854)])
- 81255 HEXA (HEXOSAMINIDASE A [ALPHA POLYPEPTIDE]) (EG, TAY-SACHS DISEASE) GENE ANALYSIS, COMMON VARIANTS (EG, 1278INSTA TC, 1421+1G>C, G269S)
- 81256 HFE (HEMOCHROMATOSIS) (EG, HEREDITARY HEMOCHROMATOSIS) GENE ANALYSIS, COMMON VARIANTS (EG, C282Y, H63D)
- 81257 HBA1/HBA2 (ALPHA GLOBIN 1 AND ALPHA GLOBIN 2) (EG, ALPHA THALASSEMIA, HB BART HYDROPS FETALIS SYNDROME, HBH DISEASE), GENE ANALYSIS, FOR COMMON DELETIONS OR

- VARIANT (EG, SOUTHEAST ASIAN, THAI, FILIPINO, MEDITERRANEAN, ALPHA3.7, ALPHA4.2, ALPHA20.5, AND CONSTANT SPRING)
- 81260 IKBKAP (INHIBITOR OF KAPPA LIGHT POLYPEPTIDE GENE ENHANCER IN B-CELLS, KINASE COMPLEX-ASSOCIATED PROTEIN) (EG, FAMILIAL DYSAUTONOMIA) GENE ANALYSIS, COMMON VARIANTS (EG, 2507+6T>C, R696P)
- 81261 IGH@ (IMMUNOGLOBULIN HEAVY CHAIN LOCUS) (EG, LEUKEMIAS AND LYMPHOMAS, B-CELL), GENE REARRANGEMENT ANALYSIS TO DETECT ABNORMAL CLONAL POPULATION(S); AMPLIFIED METHODOLOGY (EG, POLYMERASE CHAIN REACTION)
- 81262 IGH@ (IMMUNOGLOBULIN HEAVY CHAIN LOCUS) (EG, LEUKEMIAS AND LYMPHOMAS, B-CELL), GENE REARRANGEMENT ANALYSIS TO DETECT ABNORMAL CLONAL POPULATION(S); DIRECT PROBE METHODOLOGY (EG, SOUTHERN BLOT)
- 81263 IGH@ (IMMUNOGLOBULIN HEAVY CHAIN LOCUS) (EG, LEUKEMIA AND LYMPHOMA, B-CELL), VARIABLE REGION SOMATIC MUTATION ANALYSIS
- 81264 IGK@ (IMMUNOGLOBULIN KAPPA LIGHT CHAIN LOCUS) (EG, LEUKEMIA AND LYMPHOMA, B-CELL), GENE REARRANGEMENT ANALYSIS, EVALUATION TO DETECT ABNORMAL CLONAL POPULATION(S)
- 81265 COMPARATIVE ANALYSIS USING SHORT TANDEM REPEAT (STR) MARKERS; PATIENT AND COMPARATIVE SPECIMEN (EG, PRE-TRANSPLANT RECIPIENT AND DONOR GERMLINE TESTING, POST-TRANSPLANT NON-HEMATOPOIETIC RECIPIENT GERMLINE [EG, BUCCAL SWAB OR OTHER GERMLINE TISSUE SAMPLE] AND DONOR TESTING, TWIN ZYGOSITY TESTING, OR MATERNAL CELL CONTAMINATION OF FETAL CELLS)
- 81266 COMPARATIVE ANALYSIS USING SHORT TANDEM REPEAT (STR) MARKERS; EACH ADDITIONAL SPECIMEN (EG, ADDITIONAL CORD BLOOD DONOR, ADDITIONAL FETAL SAMPLES FROM DIFFERENT CULTURES, OR ADDITIONAL ZYGOSITY IN MULTIPLE BIRTH PREGNANCIES)

- (LIST SEPARATELY IN ADDITION TO CODE FOR PRIMARY PROCEDURE)
- 81267 CHIMERISM (ENGRAFTMENT) ANALYSIS, POST TRANSPLANTATION SPECIMEN (EG, HEMATOPOIETIC STEM CELL), INCLUDES COMPARISON TO PREVIOUSLY PERFORMED BASELINE ANALYSES; WITHOUT CELL SELECTION
- 81268 CHIMERISM (ENGRAFTMENT) ANALYSIS, POST TRANSPLANTATION SPECIMEN (EG, HEMATOPOIETIC STEM CELL), INCLUDES COMPARISON TO PREVIOUSLY PERFORMED BASELINE ANALYSES; WITH CELL SELECTION (EG, CD3, CD33), EACH CELL TYPE
- 81270 JAK2 (JANUS KINASE 2) (EG, MYELOPROLIFERATIVE DISORDER) GENE ANALYSIS, P.VAL617PHE (V617F) VARIANT
- 81275 KRAS (V-KI-RAS2 KIRSTEN RAT SARCOMA VIRAL ONCOGENE) (EG, CARCINOMA) GENE ANALYSIS, VARIANTS IN CODONS 12 AND 13
- 81280 LONG QT SYNDROME GENE ANALYSES (EG, KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNJ2, CACNA1C, CAV3, SCN4B, AKAP, SNTA1, AND ANK2); FULL SEQUENCE ANALYSIS
- 81281 LONG QT SYNDROME GENE ANALYSES (EG, KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNJ2, CACNA1C, CAV3, SCN4B, AKAP, SNTA1, AND ANK2); KNOWN FAMILIAL SEQUENCE VARIANT
- 81282 LONG QT SYNDROME GENE ANALYSES (EG, KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNJ2, CACNA1C, CAV3, SCN4B, AKAP, SNTA1, AND ANK2); DUPLICATION/DELETION VARIANTS
- 81287 MGMT (O-6-METHYLGUANINE-DNA METHYLTRANSFERASE) (EG, GLIOBLASTOMA MULTIFORME), METHYLATION ANALYSIS
- 81288 MLH1 (MUTL HOMOLOG 1, COLON CANCER, NONPOLYPOSIS TYPE 2) (EG, HEREDITARY NON-POLYPOSIS COLORECTAL CANCER, LYNCH SYNDROME) GENE ANALYSIS; PROMOTER METHYLATION ANALYSIS
- 81290 MCOLN1 (MUCOLIPIN 1) (EG, MUCOLIPIDOSIS, TYPE IV) GENE ANALYSIS, COMMON VARIANTS (EG, IVS3-2A>G, DEL6.4KB)
- 81291 MTHFR (5,10-METHYLENETETRAHYDROFOLATE REDUCTASE) (EG, HEREDITARY

- HYPERCOAGULABILITY) GENE ANALYSIS,
COMMON VARIANTS (EG, 677T, 1298C)
- 81292 MLH1 (MUTL HOMOLOG 1, COLON CANCER,
NONPOLYPOSIS TYPE 2) (EG, HEREDITARY NON-
POLYPOSIS COLORECTAL CANCER, LYNCH
SYNDROME) GENE ANALYSIS; FULL SEQUENCE
ANALYSIS
- 81293 MLH1 (MUTL HOMOLOG 1, COLON CANCER,
NONPOLYPOSIS TYPE 2) (EG, HEREDITARY NON-
POLYPOSIS COLORECTAL CANCER, LYNCH
SYNDROME) GENE ANALYSIS; KNOWN FAMILIAL
VARIANTS
- 81294 MLH1 (MUTL HOMOLOG 1, COLON CANCER,
NONPOLYPOSIS TYPE 2) (EG, HEREDITARY NON-
POLYPOSIS COLORECTAL CANCER, LYNCH
SYNDROME) GENE ANALYSIS;
DUPLICATION/DELETION VARIANTS
- 81295 MSH2 (MUTS HOMOLOG 2, COLON CANCER,
NONPOLYPOSIS TYPE 1) (EG, HEREDITARY NON-
POLYPOSIS COLORECTAL CANCER, LYNCH
SYNDROME) GENE ANALYSIS; FULL SEQUENCE
ANALYSIS
- 81296 MSH2 (MUTS HOMOLOG 2, COLON CANCER,
NONPOLYPOSIS TYPE 1) (EG, HEREDITARY NON-
POLYPOSIS COLORECTAL CANCER, LYNCH
SYNDROME) GENE ANALYSIS; KNOWN FAMILIAL
VARIANTS
- 81297 MSH2 (MUTS HOMOLOG 2, COLON CANCER,
NONPOLYPOSIS TYPE 1) (EG, HEREDITARY NON-
POLYPOSIS COLORECTAL CANCER, LYNCH
SYNDROME) GENE ANALYSIS;
DUPLICATION/DELETION VARIANTS
- 81298 MSH6 (MUTS HOMOLOG 6 [E. COLI]) (EG,
HEREDITARY NON-POLYPOSIS COLORECTAL
CANCER, LYNCH SYNDROME) GENE ANALYSIS;
FULL SEQUENCE ANALYSIS
- 81299 MSH6 (MUTS HOMOLOG 6 [E. COLI]) (EG,
HEREDITARY NON-POLYPOSIS COLORECTAL
CANCER, LYNCH SYNDROME) GENE ANALYSIS;
KNOWN FAMILIAL VARIANTS
- 81300 MSH6 (MUTS HOMOLOG 6 [E. COLI]) (EG,
HEREDITARY NON-POLYPOSIS COLORECTAL
CANCER, LYNCH SYNDROME) GENE ANALYSIS;
DUPLICATION/DELETION VARIANTS

- 81301 MICROSATELLITE INSTABILITY ANALYSIS (EG, HEREDITARY NON-POLYPOSIS COLORECTAL CANCER, LYNCH SYNDROME) OF MARKERS FOR MISMATCH REPAIR DEFICIENCY (EG, BAT25, BAT26), INCLUDES COMPARISON OF NEOPLASTIC AND NORMAL TISSUE, IF PERFORMED
- 81302 MECP2 (METHYL CPG BINDING PROTEIN 2) (EG, RETT SYNDROME) GENE ANALYSIS; FULL SEQUENCE ANALYSIS
- 81303 MECP2 (METHYL CPG BINDING PROTEIN 2) (EG, RETT SYNDROME) GENE ANALYSIS; KNOWN FAMILIAL VARIANT
- 81304 MECP2 (METHYL CPG BINDING PROTEIN 2) (EG, RETT SYNDROME) GENE ANALYSIS; DUPLICATION/DELETION VARIANTS
- 81310 NPM1 (NUCLEOPHOSMIN) (EG, ACUTE MYELOID LEUKEMIA) GENE ANALYSIS, EXON 12 VARIANTS
- 81313 PCA3/KLK3 (PROSTATE CANCER ANTIGEN 3 [NON-PROTEIN CODING]/KALLIKREIN-RELATED PEPTIDASE 3 [PROSTATE SPECIFIC ANTIGEN]) RATIO (EG, PROSTATE CANCER)
- 81315 PML/RARALPHA, (T(15;17)), (PROMYELOCYTIC LEUKEMIA/RETINOIC ACID RECEPTOR ALPHA) (EG, PROMYELOCYTIC LEUKEMIA) TRANSLOCATION ANALYSIS; COMMON BREAKPOINTS (EG, INTRON 3 AND INTRON 6), QUALITATIVE OR QUANTITATIVE
- 81316 PML/RARALPHA, (T(15;17)), (PROMYELOCYTIC LEUKEMIA/RETINOIC ACID RECEPTOR ALPHA) (EG, PROMYELOCYTIC LEUKEMIA) TRANSLOCATION ANALYSIS; SINGLE BREAKPOINT (EG, INTRON 3, INTRON 6 OR EXON 6), QUALITATIVE OR QUANTITATIVE
- 81317 PMS2 (POSTMEIOTIC SEGREGATION INCREASED 2 [S. CEREVISIAE]) (EG, HEREDITARY NON-POLYPOSIS COLORECTAL CANCER, LYNCH SYNDROME) GENE ANALYSIS; FULL SEQUENCE ANALYSIS
- 81318 PMS2 (POSTMEIOTIC SEGREGATION INCREASED 2 [S. CEREVISIAE]) (EG, HEREDITARY NON-POLYPOSIS COLORECTAL CANCER, LYNCH SYNDROME) GENE ANALYSIS; KNOWN FAMILIAL VARIANTS
- 81319 PMS2 (POSTMEIOTIC SEGREGATION INCREASED 2 [S. CEREVISIAE]) (EG, HEREDITARY NON-

- POLYPOSIS COLORECTAL CANCER, LYNCH SYNDROME) GENE ANALYSIS;
DUPLICATION/DELETION VARIANTS
- 81321 PTEN (PHOSPHATASE AND TENSIN HOMOLOG) (EG, COWDEN SYNDROME, PTEN HAMARTOMA TUMOR SYNDROME) GENE ANALYSIS; FULL SEQUENCE ANALYSIS
- 81322 PTEN (PHOSPHATASE AND TENSIN HOMOLOG) (EG, COWDEN SYNDROME, PTEN HAMARTOMA TUMOR SYNDROME) GENE ANALYSIS; KNOWN FAMILIAL VARIANT
- 81323 PTEN (PHOSPHATASE AND TENSIN HOMOLOG) (EG, COWDEN SYNDROME, PTEN HAMARTOMA TUMOR SYNDROME) GENE ANALYSIS;
DUPLICATION/DELETION VARIANT
- 81324 PMP22 (PERIPHERAL MYELIN PROTEIN 22) (EG, CHARCOT-MARIE-TOOTH, HEREDITARY NEUROPATHY WITH LIABILITY TO PRESSURE PALSIES) GENE ANALYSIS;
DUPLICATION/DELETION ANALYSIS
- 81325 PMP22 (PERIPHERAL MYELIN PROTEIN 22) (EG, CHARCOT-MARIE-TOOTH, HEREDITARY NEUROPATHY WITH LIABILITY TO PRESSURE PALSIES) GENE ANALYSIS; FULL SEQUENCE ANALYSIS
- 81326 PMP22 (PERIPHERAL MYELIN PROTEIN 22) (EG, CHARCOT-MARIE-TOOTH, HEREDITARY NEUROPATHY WITH LIABILITY TO PRESSURE PALSIES) GENE ANALYSIS; KNOWN FAMILIAL VARIANT
- 81330 SMPD1(SPHINGOMYELIN PHOSPHODIESTERASE 1, ACID LYSOSOMAL) (EG, NIEMANN-PICK DISEASE, TYPE A) GENE ANALYSIS, COMMON VARIANTS (EG, R496L, L302P, FSP330)
- 81331 SNRPN/UBE3A (SMALL NUCLEAR RIBONUCLEOPROTEIN POLYPEPTIDE N AND UBIQUITIN PROTEIN LIGASE E3A) (EG, PRADER-WILLI SYNDROME AND/OR ANGELMAN SYNDROME), METHYLATION ANALYSIS
- 81332 SERPINA1 (SERPIN PEPTIDASE INHIBITOR, CLADE A, ALPHA-1 ANTIPROTEINASE, ANTITRYPSIN, MEMBER 1) (EG, ALPHA-1-ANTITRYPSIN DEFICIENCY), GENE ANALYSIS, COMMON VARIANTS (EG, *S AND *Z)

- 81340 TRB@ (T CELL ANTIGEN RECEPTOR, BETA) (EG, LEUKEMIA AND LYMPHOMA), GENE REARRANGEMENT ANALYSIS TO DETECT ABNORMAL CLONAL POPULATION(S); USING AMPLIFICATION METHODOLOGY (EG, POLYMERASE CHAIN REACTION)
- 81341 TRB@ (T CELL ANTIGEN RECEPTOR, BETA) (EG, LEUKEMIA AND LYMPHOMA), GENE REARRANGEMENT ANALYSIS TO DETECT ABNORMAL CLONAL POPULATION(S); USING DIRECT PROBE METHODOLOGY (EG, SOUTHERN BLOT)
- 81342 TRG@ (T CELL ANTIGEN RECEPTOR, GAMMA) (EG, LEUKEMIA AND LYMPHOMA), GENE REARRANGEMENT ANALYSIS, EVALUATION TO DETECT ABNORMAL CLONAL POPULATION(S)
- 81350 UGT1A1 (UDP GLUCURONOSYLTRANSFERASE 1 FAMILY, POLYPEPTIDE A1) (EG, IRINOTECAN METABOLISM), GENE ANALYSIS, COMMON VARIANTS (EG, *28, *36, *37)
- 81355 VKORC1 (VITAMIN K EPOXIDE REDUCTASE COMPLEX, SUBUNIT 1) (EG, WARFARIN METABOLISM), GENE ANALYSIS, COMMON VARIANTS (EG, -1639/3673)
- 81370 HLA CLASS I AND II TYPING, LOW RESOLUTION (EG, ANTIGEN EQUIVALENTS); HLA-A, -B, -C, -DRB1/3/4/5, AND -DQB1
- 81371 HLA CLASS I AND II TYPING, LOW RESOLUTION (EG, ANTIGEN EQUIVALENTS); HLA-A, -B, AND -DRB1 (EG, VERIFICATION TYPING)
- 81372 HLA CLASS I TYPING, LOW RESOLUTION (EG, ANTIGEN EQUIVALENTS); COMPLETE (IE, HLA-A, -B, AND -C)
- 81373 HLA CLASS I TYPING, LOW RESOLUTION (EG, ANTIGEN EQUIVALENTS); ONE LOCUS (EG, HLA-A, -B, OR -C), EACH
- 81374 HLA CLASS I TYPING, LOW RESOLUTION (EG, ANTIGEN EQUIVALENTS); ONE ANTIGEN EQUIVALENT (EG, B*27), EACH
- 81375 HLA CLASS II TYPING, LOW RESOLUTION (EG, ANTIGEN EQUIVALENTS); HLA-DRB1/3/4/5 AND -DQB1
- 81376 HLA CLASS II TYPING, LOW RESOLUTION (EG, ANTIGEN EQUIVALENTS); ONE LOCUS (EG, HLA-

- DRB1, -DRB3/4/5, -DQB1, -DQA1, -DPB1, OR -DPA1), EACH
- 81377 HLA CLASS II TYPING, LOW RESOLUTION (EG, ANTIGEN EQUIVALENTS); ONE ANTIGEN EQUIVALENT, EACH
- 81378 HLA CLASS I AND II TYPING, HIGH RESOLUTION (IE, ALLELES OR ALLELE GROUPS), HLA-A, -B, -C, AND -DRB1
- 81379 HLA CLASS I TYPING, HIGH RESOLUTION (IE, ALLELES OR ALLELE GROUPS); COMPLETE (IE, HLA-A, -B, AND -C)
- 81380 HLA CLASS I TYPING, HIGH RESOLUTION (IE, ALLELES OR ALLELE GROUPS); ONE LOCUS (EG, HLA-A, -B, OR -C), EACH
- 81381 HLA CLASS I TYPING, HIGH RESOLUTION (IE, ALLELES OR ALLELE GROUPS); ONE ALLELE OR ALLELE GROUP (EG, B*57:01P), EACH
- 81382 HLA CLASS II TYPING, HIGH RESOLUTION (IE, ALLELES OR ALLELE GROUPS); ONE LOCUS (EG, HLA-DRB1, -DRB3/4/5, -DQB1, -DQA1, -DPB1, OR -DPA1), EACH
- 81383 HLA CLASS II TYPING, HIGH RESOLUTION (IE, ALLELES OR ALLELE GROUPS); ONE ALLELE OR ALLELE GROUP (EG, HLA-DQB1*06:02P), EACH
- 81400 MOLECULAR PATHOLOGY PROCEDURE, LEVEL 1 (EG, IDENTIFICATION OF SINGLE GERMLINE VARIANT [EG, SNP] BY TECHNIQUES SUCH AS RESTRICTION ENZYME DIGESTION OR MELT CURVE ANALYSIS)
- 81401 MOLECULAR PATHOLOGY PROCEDURE, LEVEL 2 (EG, 2-10 SNPS, 1 METHYLATED VARIANT, OR 1 SOMATIC VARIANT [TYPICALLY USING NONSEQUENCING TARGET VARIANT ANALYSIS], OR DETECTION OF A DYNAMIC MUTATION DISORDER/TRIPLET REPEAT)
- 81402 MOLECULAR PATHOLOGY PROCEDURE, LEVEL 3 (EG, >10 SNPS, 2-10 METHYLATED VARIANTS, OR 2-10 SOMATIC VARIANTS [TYPICALLY USING NON-SEQUENCING TARGET VARIANT ANALYSIS], IMMUNOGLOBULIN AND T-CELL RECEPTOR GENE REARRANGMENTS, DUPLICATION/DELETION VARIANTS OF 1 EXON, LOSS OF HETEROZYGOSITY [LOH], UNIPARENTAL DISOMY [UPD])

- 81403 MOLECULAR PATHOLOGY PROCEDURE, LEVEL 4 (EG, ANALYSIS OF SINGLE EXON BY DNA SEQUENCE ANALYSIS, ANALYSIS OF >10 AMPLICONS USING MULTIPLEX PCR IN 2 OR MORE INDEPENDENT REACTIONS, MUTATION SCANNING OR DUPLICATION/DELETION VARIANTS OF 2-5 EXONS)
- 81404 MOLECULAR PATHOLOGY PROCEDURE, LEVEL 5 (EG, ANALYSIS OF 2-5 EXONS BY DNA SEQUENCE ANALYSIS, MUTATION SCANNING OR DUPLICATION/DELETION VARIANTS OF 6-10 EXONS, OR CHARACTERIZATION OF A DYNAMIC MUTATION DISORDER/TRIPLET REPEAT BY SOUTHERN BLOT ANALYSIS)
- 81405 MOLECULAR PATHOLOGY PROCEDURE, LEVEL 6 (EG, ANALYSIS OF 6-10 EXONS BY DNA SEQUENCE ANALYSIS, MUTATION SCANNING OR DUPLICATION/DELETION VARIANTS OF 11-25 EXONS)
- 81406 MOLECULAR PATHOLOGY PROCEDURE, LEVEL 7 (EG, ANALYSIS OF 11-25 EXONS BY DNA SEQUENCE ANALYSIS, MUTATION SCANNING OR DUPLICATION/DELETION VARIANTS OF 26-50 EXONS, CYTOGENOMIC ARRAY ANALYSIS FOR NEOPLASIA)
- 81407 MOLECULAR PATHOLOGY PROCEDURE, LEVEL 8 (EG, ANALYSIS OF 26-50 EXONS BY DNA SEQUENCE ANALYSIS, MUTATION SCANNING OR DUPLICATION/DELETION VARIANTS OF >50 EXONS, SEQUENCE ANALYSIS OF MULTIPLE GENES ON ONE PLATFORM)
- 81408 MOLECULAR PATHOLOGY PROCEDURE, LEVEL 9 (EG, ANALYSIS OF >50 EXONS IN A SINGLE GENE BY DNA SEQUENCE ANALYSIS)
- 81410 AORTIC DYSFUNCTION OR DILATION (EG, MARFAN SYNDROME, LOEYS DIETZ SYNDROME, EHLER DANLOS SYNDROME TYPE IV, ARTERIAL TORTUOSITY SYNDROME); GENOMIC SEQUENCE ANALYSIS PANEL, MUST INCLUDE SEQUENCING OF AT LEAST 9 GENES, INCLUDING FBN1, TGFBR1, TGFBR2, COL3A1, MYH11, ACTA2, SLC2A10, SMAD3, AND MYLK
- 81411 AORTIC DYSFUNCTION OR DILATION (EG, MARFAN SYNDROME, LOEYS DIETZ SYNDROME, EHLER DANLOS SYNDROME TYPE IV, ARTERIAL

- TORTUOSITY SYNDROME);
 DUPLICATION/DELETION ANALYSIS PANEL, MUST
 INCLUDE ANALYSES FOR TGFBR1, TGFBR2,
 MYH11, AND COL3A1
- 81415 EXOME (EG, UNEXPLAINED CONSTITUTIONAL OR
 HERITABLE DISORDER OR SYNDROME);
 SEQUENCE ANALYSIS
- 81416 EXOME (EG, UNEXPLAINED CONSTITUTIONAL OR
 HERITABLE DISORDER OR SYNDROME);
 SEQUENCE ANALYSIS, EACH COMPARATOR
 EXOME (EG, PARENTS, SIBLINGS) (LIST
 SEPARATELY IN ADDITION TO CODE FOR
 PRIMARY PROCEDURE)
- 81417 EXOME (EG, UNEXPLAINED CONSTITUTIONAL OR
 HERITABLE DISORDER OR SYNDROME); RE-
 EVALUATION OF PREVIOUSLY OBTAINED EXOME
 SEQUENCE (EG, UPDATED KNOWLEDGE OR
 UNRELATED CONDITION/SYNDROME)
- 81420 FETAL CHROMOSOMAL ANEUPLOIDY (EG,
 TRISOMY 21, MONOSOMY X) GENOMIC SEQUENCE
 ANALYSIS PANEL, CIRCULATING CELL-FREE
 FETAL DNA IN MATERNAL BLOOD, MUST INCLUDE
 ANALYSIS OF CHROMOSOMES 13, 18, AND 21
- 81425 GENOME (EG, UNEXPLAINED CONSTITUTIONAL OR
 HERITABLE DISORDER OR SYNDROME);
 SEQUENCE ANALYSIS
- 81426 GENOME (EG, UNEXPLAINED CONSTITUTIONAL OR
 HERITABLE DISORDER OR SYNDROME);
 SEQUENCE ANALYSIS, EACH COMPARATOR
 GENOME (EG, PARENTS, SIBLINGS) (LIST
 SEPARATELY IN ADDITION TO CODE FOR
 PRIMARY PROCEDURE)
- 81427 GENOME (EG, UNEXPLAINED CONSTITUTIONAL OR
 HERITABLE DISORDER OR SYNDROME); RE-
 EVALUATION OF PREVIOUSLY OBTAINED
 GENOME SEQUENCE (EG, UPDATED KNOWLEDGE
 OR UNRELATED CONDITION/SYNDROME)
- 81430 HEARING LOSS (EG, NONSYNDROMIC HEARING
 LOSS, USHER SYNDROME, PENDRED SYNDROME);
 GENOMIC SEQUENCE ANALYSIS PANEL, MUST
 INCLUDE SEQUENCING OF AT LEAST 60 GENES,
 INCLUDING CDH23, CLRN1, GJB2, GPR98, MTRNR1,
 MYO7A, MYO15A, PCDH15, OTOF, SLC26A4, TMC1,
 TMPRSS3, USH1C, USH1G, USH2A, AND WFS1

- 81431 HEARING LOSS (EG, NONSYNDROMIC HEARING LOSS, USHER SYNDROME, PENDRED SYNDROME); DUPLICATION/DELETION ANALYSIS PANEL, MUST INCLUDE COPY NUMBER ANALYSES FOR STRC AND DFNB1 DELETIONS IN GJB2 AND GJB6 GENES
- 81435 HEREDITARY COLON CANCER SYNDROMES (EG, LYNCH SYNDROME, FAMILIAL ADENOMATOSIS POLYPOSIS); GENOMIC SEQUENCE ANALYSIS PANEL, MUST INCLUDE ANALYSIS OF AT LEAST 7 GENES, INCLUDING APC, CHEK2, MLH1, MSH2, MSH6, MUTYH, AND PMS2
- 81436 HEREDITARY COLON CANCER SYNDROMES (EG, LYNCH SYNDROME, FAMILIAL ADENOMATOSIS POLYPOSIS); DUPLICATION/DELETION GENE ANALYSIS PANEL, MUST INCLUDE ANALYSIS OF AT LEAST 8 GENES, INCLUDING APC, MLH1, MSH2, MSH6, PMS2, EPCAM, CHEK2, AND MUTYH
- 81440 NUCLEAR ENCODED MITOCHONDRIAL GENES (EG, NEUROLOGIC OR MYOPATHIC PHENOTYPES), GENOMIC SEQUENCE PANEL, MUST INCLUDE ANALYSIS OF AT LEAST 100 GENES, INCLUDING BCS1L, C10ORF2, COQ2, COX10, DGUOK, MPV17, OPA1, PDSS2, POLG, POLG2, RRM2B, SCO1, SCO2, SLC25A4, SUCLA2, SUCLG1, TAZ, TK2, AND TYMP
- 81445 TARGETED GENOMIC SEQUENCE ANALYSIS PANEL, SOLID ORGAN NEOPLASM, DNA ANALYSIS, 5-50 GENES (EG, ALK, BRAF, CDKN2A, EGFR, ERBB2, KIT, KRAS, NRAS, MET, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), INTERROGATION FOR SEQUENCE VARIANTS AND COPY NUMBER VARIANTS OR REARRANGEMENTS, IF PERFORMED
- 81450 TARGETED GENOMIC SEQUENCE ANALYSIS PANEL, HEMATOLYMPHOID NEOPLASM OR DISORDER, DNA AND RNA ANALYSIS WHEN PERFORMED, 5-50 GENES (EG, BRAF, CEBPA, DNMT3A, EZH2, FLT3, IDH1, IDH2, JAK2, KRAS, KIT, MLL, NRAS, NPM1, NOTCH1), INTERROGATION FOR SEQUENCE VARIANTS, AND COPY NUMBER VARIANTS OR REARRANGEMENTS, OR ISOFORM EXPRESSION OR MRNA EXPRESSION LEVELS, IF PERFORMED
- 81455 TARGETED GENOMIC SEQUENCE ANALYSIS PANEL, SOLID ORGAN OR HEMATOLYMPHOID NEOPLASM, DNA AND RNA ANALYSIS WHEN PERFORMED, 51 OR GREATER GENES (EG, ALK,

BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MLL, NPM1, NRAS, MET, NOTCH1, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), INTERROGATION FOR SEQUENCE VARIANTS AND COPY NUMBER VARIANTS OR REARRANGEMENTS, IF PERFORMED

81460 WHOLE MITOCHONDRIAL GENOME (EG, LEIGH SYNDROME, MITOCHONDRIAL ENCEPHALOMYOPATHY, LACTIC ACIDOSIS, AND STROKE-LIKE EPISODES [MELAS], MYOCLONIC EPILEPSY WITH RAGGED-RED FIBERS [MERFF], NEUROPATHY, ATAXIA, AND RETINITIS PIGMENTOSA [NARP], LEBER HEREDITARY OPTIC NEUROPATHY [LHON]), GENOMIC SEQUENCE, MUST INCLUDE SEQUENCE ANALYSIS OF ENTIRE MITOCHONDRIAL GENOME WITH HETEROPLASMY DETECTION

81465 WHOLE MITOCHONDRIAL GENOME LARGE DELETION ANALYSIS PANEL (EG, KEARNS-SAYRE SYNDROME, CHRONIC PROGRESSIVE EXTERNAL OPHTHALMOPLEGIA), INCLUDING HETEROPLASMY DETECTION, IF PERFORMED

81470 X-LINKED INTELLECTUAL DISABILITY (XLID) (EG, SYNDROMIC AND NON-SYNDROMIC XLID); GENOMIC SEQUENCE ANALYSIS PANEL, MUST INCLUDE SEQUENCING OF AT LEAST 60 GENES, INCLUDING ARX, ATRX, CDKL5, FGD1, FMR1, HUWE1, IL1RAPL, KDM5C, L1CAM, MECP2, MED12, MID1, OCRL, RPS6KA3, AND SLC16A2

81471 X-LINKED INTELLECTUAL DISABILITY (XLID) (EG, SYNDROMIC AND NON-SYNDROMIC XLID); DUPLICATION/DELETION GENE ANALYSIS, MUST INCLUDE ANALYSIS OF AT LEAST 60 GENES, INCLUDING ARX, ATRX, CDKL5, FGD1, FMR1, HUWE1, IL1RAPL, KDM5C, L1CAM, MECP2, MED12, MID1, OCRL, RPS6KA3, AND SLC16A2

81479 UNLISTED MOLECULAR PATHOLOGY PROCEDURE

82172 APOLIPOPROTEIN, EACH

82306 VITAMIN D; 25 HYDROXY, INCLUDES FRACTION(S), IF PERFORMED

82610 CYSTATIN C

82725 FATTY ACIDS, NONESTERIFIED

82726 VERY LONG CHAIN FATTY ACIDS

82977 GLUTAMYLTRANSFERASE, GAMMA (GGT)

83090	HOMOCYSTEINE
83695	LIPOPROTEIN (A)
83698	LIPOPROTEIN-ASSOCIATED PHOSPHOLIPASE A2 (LP-PLA2)
83700	LIPOPROTEIN, BLOOD; ELECTROPHORETIC SEPARATION AND QUANTITATION
83701	LIPOPROTEIN, BLOOD; HIGH RESOLUTION FRACTIONATION AND QUANTITATION OF LIPOPROTEINS INCLUDING LIPOPROTEIN SUBCLASSES WHEN PERFORMED (EG, ELECTROPHORESIS, ULTRACENTRIFUGATION)
83704	LIPOPROTEIN, BLOOD; QUANTITATION OF LIPOPROTEIN PARTICLE NUMBERS AND LIPOPROTEIN PARTICLE SUBCLASSES (EG, BY NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY)
83719	LIPOPROTEIN, DIRECT MEASUREMENT; VLDL CHOLESTEROL
83721	LIPOPROTEIN, DIRECT MEASUREMENT; LDL CHOLESTEROL
83876	MYELOPEROXIDASE (MPO)
83880	NATRIURETIC PEPTIDE
84999	UNLISTED CHEMISTRY PROCEDURE
85230	CLOTTING; FACTOR VII (PROCONVERTIN, STABLE FACTOR)
85246	CLOTTING; FACTOR VIII, VW FACTOR ANTIGEN
85301	CLOTTING INHIBITORS OR ANTICOAGULANTS; ANTITHROMBIN III, ANTIGEN ASSAY
85302	CLOTTING INHIBITORS OR ANTICOAGULANTS; PROTEIN C, ANTIGEN
85378	FIBRIN DEGRADATION PRODUCTS, D-DIMER; QUALITATIVE OR SEMIQUANTITATIVE
85384	FIBRINOGEN; ACTIVITY
85415	FIBRINOLYTIC FACTORS AND INHIBITORS; PLASMINOGEN ACTIVATOR
86140	C-REACTIVE PROTEIN;
0111T	LONG-CHAIN (C20-22) OMEGA-3 FATTY ACIDS IN RED BLOOD CELL (RBC) MEMBRANES

**Does the CPT
30% Coding
Rule Apply?**

No

Group 1: Paragraph

The following ICD-10 codes are covered:

Group 1: Codes

E71.30	Disorder of fatty-acid metabolism, unspecified
E75.21	Fabry (-Anderson) disease
E75.22	Gaucher disease
E75.240	Niemann-Pick disease type A
E75.241	Niemann-Pick disease type B
E75.242	Niemann-Pick disease type C
E75.243	Niemann-Pick disease type D
E75.248	Other Niemann-Pick disease
E75.249	Niemann-Pick disease, unspecified
E75.3	Sphingolipidosis, unspecified
E75.5	Other lipid storage disorders
E75.6	Lipid storage disorder, unspecified
E77.0	Defects in post-translational modification of lysosomal enzymes
E77.8	Other disorders of glycoprotein metabolism
E77.9	Disorder of glycoprotein metabolism, unspecified
E78.0	Pure hypercholesterolemia
E78.1	Pure hyperglyceridemia
E78.2	Mixed hyperlipidemia
E78.3	Hyperchylomicronemia
E78.4	Other hyperlipidemia
E78.5	Hyperlipidemia, unspecified
E78.70	Disorder of bile acid and cholesterol metabolism, unspecified
E78.79	Other disorders of bile acid and cholesterol metabolism
E78.81	Lipoid dermatoarthritis
E78.89	Other lipoprotein metabolism disorders
E78.9	Disorder of lipoprotein metabolism, unspecified
E88.1	Lipodystrophy, not elsewhere classified
E88.2	Lipomatosis, not elsewhere classified
E88.89	Other specified metabolic disorders
I10	Essential (primary) hypertension
I20.0	Unstable angina
I20.1	Angina pectoris with documented spasm
I20.8	Other forms of angina pectoris
I20.9	Angina pectoris, unspecified

**ICD-10 Codes
that Support
Medical
Necessity**

**Note:
Performance is
optimized by
using code
ranges.**

I21.01	ST elevation (STEMI) myocardial infarction involving left main coronary artery
I21.02	ST elevation (STEMI) myocardial infarction involving left anterior descending coronary artery
I21.09	ST elevation (STEMI) myocardial infarction involving other coronary artery of anterior wall
I21.11	ST elevation (STEMI) myocardial infarction involving right coronary artery
I21.19	ST elevation (STEMI) myocardial infarction involving other coronary artery of inferior wall
I21.21	ST elevation (STEMI) myocardial infarction involving left circumflex coronary artery
I21.29	ST elevation (STEMI) myocardial infarction involving other sites
I21.3	ST elevation (STEMI) myocardial infarction of unspecified site
I21.4	Non-ST elevation (NSTEMI) myocardial infarction
I22.0	Subsequent ST elevation (STEMI) myocardial infarction of anterior wall
I22.1	Subsequent ST elevation (STEMI) myocardial infarction of inferior wall
I22.2	Subsequent non-ST elevation (NSTEMI) myocardial infarction
I22.8	Subsequent ST elevation (STEMI) myocardial infarction of other sites
I22.9	Subsequent ST elevation (STEMI) myocardial infarction of unspecified site
I24.0	Acute coronary thrombosis not resulting in myocardial infarction
I24.1	Dressler's syndrome
I24.8	Other forms of acute ischemic heart disease
I24.9	Acute ischemic heart disease, unspecified
I25.10	Atherosclerotic heart disease of native coronary artery without angina pectoris
I25.110	Atherosclerotic heart disease of native coronary artery with unstable angina pectoris
I25.111	Atherosclerotic heart disease of native coronary artery with angina pectoris with documented spasm
I25.118	Atherosclerotic heart disease of native coronary artery with other forms of angina pectoris

I25.119	Atherosclerotic heart disease of native coronary artery with unspecified angina pectoris
I25.2	Old myocardial infarction
I25.3	Aneurysm of heart
I25.5	Ischemic cardiomyopathy
I25.6	Silent myocardial ischemia
I25.700	Atherosclerosis of coronary artery bypass graft(s), unspecified, with unstable angina pectoris
I25.701	Atherosclerosis of coronary artery bypass graft(s), unspecified, with angina pectoris with documented spasm
I25.708	Atherosclerosis of coronary artery bypass graft(s), unspecified, with other forms of angina pectoris
I25.709	Atherosclerosis of coronary artery bypass graft(s), unspecified, with unspecified angina pectoris
I25.710	Atherosclerosis of autologous vein coronary artery bypass graft(s) with unstable angina pectoris
I25.711	Atherosclerosis of autologous vein coronary artery bypass graft(s) with angina pectoris with documented spasm
I25.718	Atherosclerosis of autologous vein coronary artery bypass graft(s) with other forms of angina pectoris
I25.719	Atherosclerosis of autologous vein coronary artery bypass graft(s) with unspecified angina pectoris
I25.720	Atherosclerosis of autologous artery coronary artery bypass graft(s) with unstable angina pectoris
I25.721	Atherosclerosis of autologous artery coronary artery bypass graft(s) with angina pectoris with documented spasm
I25.728	Atherosclerosis of autologous artery coronary artery bypass graft(s) with other forms of angina pectoris
I25.729	Atherosclerosis of autologous artery coronary artery bypass graft(s) with unspecified angina pectoris
I25.730	Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with unstable angina pectoris
I25.731	Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with angina pectoris with documented spasm
I25.738	Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with other forms of angina pectoris
I25.739	Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with unspecified angina pectoris
I25.750	Atherosclerosis of native coronary artery of transplanted heart with unstable angina

I25.751	Atherosclerosis of native coronary artery of transplanted heart with angina pectoris with documented spasm
I25.758	Atherosclerosis of native coronary artery of transplanted heart with other forms of angina pectoris
I25.759	Atherosclerosis of native coronary artery of transplanted heart with unspecified angina pectoris
I25.760	Atherosclerosis of bypass graft of coronary artery of transplanted heart with unstable angina
I25.761	Atherosclerosis of bypass graft of coronary artery of transplanted heart with angina pectoris with documented spasm
I25.768	Atherosclerosis of bypass graft of coronary artery of transplanted heart with other forms of angina pectoris
I25.769	Atherosclerosis of bypass graft of coronary artery of transplanted heart with unspecified angina pectoris
I25.790	Atherosclerosis of other coronary artery bypass graft(s) with unstable angina pectoris
I25.791	Atherosclerosis of other coronary artery bypass graft(s) with angina pectoris with documented spasm
I25.798	Atherosclerosis of other coronary artery bypass graft(s) with other forms of angina pectoris
I25.799	Atherosclerosis of other coronary artery bypass graft(s) with unspecified angina pectoris
I25.810	Atherosclerosis of coronary artery bypass graft(s) without angina pectoris
I25.811	Atherosclerosis of native coronary artery of transplanted heart without angina pectoris
I25.812	Atherosclerosis of bypass graft of coronary artery of transplanted heart without angina pectoris
I25.82	Chronic total occlusion of coronary artery
I25.83	Coronary atherosclerosis due to lipid rich plaque
I25.84	Coronary atherosclerosis due to calcified coronary lesion
I25.89	Other forms of chronic ischemic heart disease
I25.9	Chronic ischemic heart disease, unspecified
I48.0	Paroxysmal atrial fibrillation
I48.1	Persistent atrial fibrillation
I48.2	Chronic atrial fibrillation
I48.3	Typical atrial flutter
I48.4	Atypical atrial flutter
I48.91	Unspecified atrial fibrillation
I48.92	Unspecified atrial flutter

I51.9	Heart disease, unspecified
I70.0	Atherosclerosis of aorta
I70.92	Chronic total occlusion of artery of the extremities

Group 1: Paragraph

The following ICD-10 codes are not covered:

Group 1: Codes

E71.30	Disorder of fatty-acid metabolism, unspecified
E75.21	Fabry (-Anderson) disease
E75.22	Gaucher disease
E75.240	Niemann-Pick disease type A
E75.241	Niemann-Pick disease type B
E75.242	Niemann-Pick disease type C
E75.243	Niemann-Pick disease type D
E75.248	Other Niemann-Pick disease
E75.249	Niemann-Pick disease, unspecified
E75.3	Sphingolipidosis, unspecified
E75.5	Other lipid storage disorders
E75.6	Lipid storage disorder, unspecified
E77.0	Defects in post-translational modification of lysosomal enzymes
E77.8	Other disorders of glycoprotein metabolism
E77.9	Disorder of glycoprotein metabolism, unspecified
E78.0	Pure hypercholesterolemia
E78.1	Pure hyperglyceridemia
E78.2	Mixed hyperlipidemia
E78.3	Hyperchylomicronemia
E78.4	Other hyperlipidemia
E78.5	Hyperlipidemia, unspecified
E78.70	Disorder of bile acid and cholesterol metabolism, unspecified
E78.79	Other disorders of bile acid and cholesterol metabolism
E78.81	Lipoid dermatoarthritis
E78.89	Other lipoprotein metabolism disorders
E78.9	Disorder of lipoprotein metabolism, unspecified
E88.1	Lipodystrophy, not elsewhere classified
E88.2	Lipomatosis, not elsewhere classified
E88.89	Other specified metabolic disorders
I10	Essential (primary) hypertension

**ICD-10 Codes
that DO NOT
Support Medical
Necessity**

**Note:
Performance is
optimized by
using code
ranges.**

I25.10	Atherosclerotic heart disease of native coronary artery without angina pectoris
I42.0	Dilated cardiomyopathy
I48.2	Chronic atrial fibrillation
I48.91	Unspecified atrial fibrillation
I51.9	Heart disease, unspecified
I52	Other heart disorders in diseases classified elsewhere
I70.0	Atherosclerosis of aorta
I70.1	Atherosclerosis of renal artery
I70.201	Unspecified atherosclerosis of native arteries of extremities, right leg
I70.202	Unspecified atherosclerosis of native arteries of extremities, left leg
I70.203	Unspecified atherosclerosis of native arteries of extremities, bilateral legs
I70.208	Unspecified atherosclerosis of native arteries of extremities, other extremity
I70.209	Unspecified atherosclerosis of native arteries of extremities, unspecified extremity
I70.211	Atherosclerosis of native arteries of extremities with intermittent claudication, right leg
I70.212	Atherosclerosis of native arteries of extremities with intermittent claudication, left leg
I70.213	Atherosclerosis of native arteries of extremities with intermittent claudication, bilateral legs
I70.218	Atherosclerosis of native arteries of extremities with intermittent claudication, other extremity
I70.219	Atherosclerosis of native arteries of extremities with intermittent claudication, unspecified extremity
I70.221	Atherosclerosis of native arteries of extremities with rest pain, right leg
I70.222	Atherosclerosis of native arteries of extremities with rest pain, left leg
I70.223	Atherosclerosis of native arteries of extremities with rest pain, bilateral legs
I70.228	Atherosclerosis of native arteries of extremities with rest pain, other extremity
I70.229	Atherosclerosis of native arteries of extremities with rest pain, unspecified extremity
I70.231	Atherosclerosis of native arteries of right leg with ulceration of thigh

I70.232	Atherosclerosis of native arteries of right leg with ulceration of calf
I70.233	Atherosclerosis of native arteries of right leg with ulceration of ankle
I70.234	Atherosclerosis of native arteries of right leg with ulceration of heel and midfoot
I70.235	Atherosclerosis of native arteries of right leg with ulceration of other part of foot
I70.238	Atherosclerosis of native arteries of right leg with ulceration of other part of lower right leg
I70.239	Atherosclerosis of native arteries of right leg with ulceration of unspecified site
I70.241	Atherosclerosis of native arteries of left leg with ulceration of thigh
I70.242	Atherosclerosis of native arteries of left leg with ulceration of calf
I70.243	Atherosclerosis of native arteries of left leg with ulceration of ankle
I70.244	Atherosclerosis of native arteries of left leg with ulceration of heel and midfoot
I70.245	Atherosclerosis of native arteries of left leg with ulceration of other part of foot
I70.248	Atherosclerosis of native arteries of left leg with ulceration of other part of lower left leg
I70.249	Atherosclerosis of native arteries of left leg with ulceration of unspecified site
I70.25	Atherosclerosis of native arteries of other extremities with ulceration
I70.261	Atherosclerosis of native arteries of extremities with gangrene, right leg
I70.262	Atherosclerosis of native arteries of extremities with gangrene, left leg
I70.263	Atherosclerosis of native arteries of extremities with gangrene, bilateral legs
I70.268	Atherosclerosis of native arteries of extremities with gangrene, other extremity
I70.269	Atherosclerosis of native arteries of extremities with gangrene, unspecified extremity
I70.291	Other atherosclerosis of native arteries of extremities, right leg
I70.292	Other atherosclerosis of native arteries of extremities, left leg

I70.293	Other atherosclerosis of native arteries of extremities, bilateral legs
I70.298	Other atherosclerosis of native arteries of extremities, other extremity
I70.299	Other atherosclerosis of native arteries of extremities, unspecified extremity
I70.301	Unspecified atherosclerosis of unspecified type of bypass graft(s) of the extremities, right leg
I70.302	Unspecified atherosclerosis of unspecified type of bypass graft(s) of the extremities, left leg
I70.303	Unspecified atherosclerosis of unspecified type of bypass graft(s) of the extremities, bilateral legs
I70.308	Unspecified atherosclerosis of unspecified type of bypass graft(s) of the extremities, other extremity
I70.309	Unspecified atherosclerosis of unspecified type of bypass graft(s) of the extremities, unspecified extremity
I70.311	Atherosclerosis of unspecified type of bypass graft(s) of the extremities with intermittent claudication, right leg
I70.312	Atherosclerosis of unspecified type of bypass graft(s) of the extremities with intermittent claudication, left leg
I70.313	Atherosclerosis of unspecified type of bypass graft(s) of the extremities with intermittent claudication, bilateral legs
I70.318	Atherosclerosis of unspecified type of bypass graft(s) of the extremities with intermittent claudication, other extremity
I70.319	Atherosclerosis of unspecified type of bypass graft(s) of the extremities with intermittent claudication, unspecified extremity
I70.321	Atherosclerosis of unspecified type of bypass graft(s) of the extremities with rest pain, right leg
I70.322	Atherosclerosis of unspecified type of bypass graft(s) of the extremities with rest pain, left leg
I70.323	Atherosclerosis of unspecified type of bypass graft(s) of the extremities with rest pain, bilateral legs
I70.328	Atherosclerosis of unspecified type of bypass graft(s) of the extremities with rest pain, other extremity
I70.329	Atherosclerosis of unspecified type of bypass graft(s) of the extremities with rest pain, unspecified extremity
I70.331	Atherosclerosis of unspecified type of bypass graft(s) of the right leg with ulceration of thigh
I70.332	Atherosclerosis of unspecified type of bypass graft(s) of the right leg with ulceration of calf

I70.333	Atherosclerosis of unspecified type of bypass graft(s) of the right leg with ulceration of ankle
I70.334	Atherosclerosis of unspecified type of bypass graft(s) of the right leg with ulceration of heel and midfoot
I70.335	Atherosclerosis of unspecified type of bypass graft(s) of the right leg with ulceration of other part of foot
I70.8	Atherosclerosis of other arteries
I70.90	Unspecified atherosclerosis
I70.91	Generalized atherosclerosis
I70.92	Chronic total occlusion of artery of the extremities
R00.2	Palpitations
R07.1	Chest pain on breathing
R07.2	Precordial pain
R07.82	Intercostal pain
R07.89	Other chest pain
R07.9	Chest pain, unspecified
Z13.220	Encounter for screening for lipid disorders
Z13.6	Encounter for screening for cardiovascular disorders
Z82.41	Family history of sudden cardiac death
Z82.49	Family history of ischemic heart disease and other diseases of the circulatory system
Z86.711	Personal history of pulmonary embolism
Z86.718	Personal history of other venous thrombosis and embolism
Z86.72	Personal history of thrombophlebitis
Z86.73	Personal history of transient ischemic attack (TIA), and cerebral infarction without residual deficits
Z86.74	Personal history of sudden cardiac arrest
Z86.79	Personal history of other diseases of the circulatory system

Additional ICD-10 Information

Associated Documents



- Attachments** There are no attachments for this LCD.
- Related Local Coverage Documents** This LCD version has no Related Local Coverage Documents.
- Related National Coverage Documents** This LCD version has no Related National Coverage Documents.

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All Versions

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