The following Protocol contains medical necessity criteria that apply for this service. It is applicable to Medicare Advantage products unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. **Preauthorization is not required.** Please note that payment for covered services is subject to eligibility and the limitations noted in the patient’s contract at the time the services are rendered.

**Description**

The expression levels of various genes in circulating white blood cell or whole blood samples have been reported to discriminate between cases of obstructive coronary artery disease (CAD) and healthy controls. Multiplex gene expression testing can be combined with other risk factors to predict the likelihood of obstructive CAD in patients who present with chest pain or other suggestive symptoms, or in asymptomatic patients who are at high risk of CAD.

**Background**

Heart disease is the leading cause of death in the U.S. and, together with cerebrovascular disease, accounted for 31% of deaths in 2007. (1) Individuals with signs and symptoms of obstructive coronary artery disease (CAD), the result of a chronic inflammatory process that ultimately results in progressive luminal narrowing and acute coronary syndromes, may be evaluated with a variety of tests according to prior risk. Coronary angiography is the gold standard for diagnosing obstructive CAD, but it is invasive and associated with a low but finite risk of harm. Thus, coronary angiography is recommended for patients at a high prior risk of CAD according to history, physical findings, electrocardiogram, and biomarkers of cardiac injury. (2) For patients initially assessed at low to intermediate risk, observation and noninvasive diagnostic methods, which may include imaging methods such as coronary computed tomographic angiography (CTA), may be recommended. Nevertheless, even noninvasive imaging methods have potential risks of exposure to radiation and contrast material. In addition, coronary angiography has a relatively low yield despite risk stratification recommendations. In one study of nearly 400,000 patients without known CAD undergoing elective coronary angiography, approximately 38% were positive for obstructive CAD (using the CAD definition, stenosis of 50% or more of the diameter of the left main coronary artery or stenosis of 70% or more of the diameter of a major epicardial or branch vessel that was more than 2.0 mm in diameter; result was 41% if using the broader definition, stenosis of 50% or more in any coronary vessel). (3) Thus, methods of improving patient risk prediction before diagnostic testing are needed.

A CAD classifier has been developed based on expression levels, in whole blood samples, of 23 genes plus patient age and sex. This information is combined in an algorithm to produce a score from one to 40, with higher values associated with a higher likelihood of obstructive CAD. The test is marketed as Corus CAD™ (CardioDx, Inc.; Palo Alto, California). The intended population is stable, non-diabetic patients suspected of CAD either because of symptoms, a high-risk history, or a recent positive or inconclusive test result by conventional methods.

**Regulatory Status**

The Corus CAD™ test is not a manufactured test kit and has not been reviewed by the U.S. Food and Drug
Protocol
Gene Expression Testing to Predict Coronary Artery Disease

Administration (FDA). Rather, it is a laboratory-developed test (LDT), offered by the Clinical Laboratory Improvement Act (CLIA)-licensed CardioDx Commercial Laboratory.

Related Protocols
KIF6 Genotyping for Predicting Cardiovascular Risk and/or Effectiveness of Statin Therapy
Genotyping for 9p21 Single Nucleotide Polymorphisms to Predict Risk of Cardiovascular Disease or Aneurysm

Policy (Formerly Corporate Medical Guideline)
Gene expression testing to predict coronary artery disease (CAD) is considered investigational for all indications, including but not limited to prediction of the likelihood of CAD in stable, nondiabetic patients.

Medicare Advantage
For Medicare Advantage members this test may be medically necessary in members whom meet the developers test indications: stable, nondiabetic patients suspected of CAD either because of symptoms, a high-risk history, or a recent positive or inclusive test result by conventional methods.

Typical Symptoms are any of the following:
- Shortness of breath
- Unspecified chest pain
- Precordial pain
- Other chest pain; discomfort, pressure, tightness in chest
- Angina decubitus
- Prinzmetal angina; variant angina pectoris
- Other and unspecified angina pectoris

Atypical symptoms are any of the following, combined with one of the common CAD risk factors must also be present:
- Backache unspecified; acute or chronic pain located in posterior region of thorax, lumbosacral region or adjacent regions
- Dizziness; light-headedness
- Other malaise and fatigue; lethargy; tiredness
- Palpitations; awareness of heart beat
- Nausea with vomiting
- Nausea alone
- Vomiting alone
- Heartburn
- Abdominal pain

Common CAD Risk Factors, combined with one of the atypical symptoms:
- Hypercholesterolemia
- Hyperglyceridemia
- Hyperlipidemia, mixed
• Hyperlipidemia, other and unspecified
• Dysmetabolic syndrome X
• Obesity
• Obesity, morbid
• Tobacco use disorder; tobacco dependence
• Essential hypertension, benign
• Essential hypertension, unspecified
• Coronary atherosclerosis of native coronary artery
• Occlusion and stenosis of carotid artery
• Cerebral atherosclerosis
• Atherosclerosis of the aorta
• Atherosclerosis of the renal artery
• Atherosclerosis of native arteries of the extremities
• Family history of ischemic heart disease
• Family history of sudden cardiac death
• Tobacco use, history: Female age 60 or more, Male age 50 or more

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. Some of this Protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.

References
We are not responsible for the continuing viability of web site addresses that may be listed in any references below.


17. Palmetto GBA Medicare Contractor (Primary Geographic Jurisdiction California – Northern, California – Southern, American Samoa, Guam, Hawaii, Northern Mariana Islands, Nevada) (North Carolina, South
Carolina, West Virginia, Virginia) Local Coverage Article: MolDX: Corus® CAD Test Coding and Billing Guidelines (A51927), Revision Effective Date 04/04/2014.