CareSource

MEDICAL POLICY STATEMENT
OHIO MEDICAID

Policy Name	Policy Number	Date Effective
Cardiovascular Disease Risk Testing	MM-1141	6/1/2021-06/30/2021

Policy Type			
MEDICAL	Administrative	Pharmacy	Reimbursement

Medical Policy Statement prepared by CareSource and its affiliates are derived from literature based on and supported by clinical guidelines, nationally recognized utilization and technology assessment guidelines, other medical management industry standards, and published MCO clinical policy guidelines. Medically necessary services include, but are not limited to, those health care services or supplies that are proper and necessary for the diagnosis or treatment of disease, illness, or injury and without which the patient can be expected to suffer prolonged, increased or new morbidity, impairment of function, dysfunction of a body organ or part, or significant pain and discomfort. These services meet the standards of good medical practice in the local area, are the lowest cost alternative, and are not provided mainly for the convenience of the member or provider. Medically necessary services also include those services defined in any Evidence of Coverage documents, Medical Policy Statements, Provider Manuals, Member Handbooks, and/or other policies and procedures.

Medical Policy Statements prepared by CareSource and its affiliates do not ensure an authorization or payment of services. Please refer to the plan contract (often referred to as the Evidence of Coverage) for the service(s) referenced in the Medical Policy Statement. If there is a conflict between the Medical Policy Statement and the plan contract (i.e., Evidence of Coverage), then the plan contract (i.e., Evidence of Coverage) will be the controlling document used to make the determination.

According to the rules of Mental Health Parity Addiction Equity Act (MHPAEA), coverage for the diagnosis and treatment of a behavioral health disorder will not be subject to any limitations that are less favorable than the limitations that apply to medical conditions as covered under this policy.

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A. Subject

Cardiovascular Disease Risk Testing

B. Background

Cardiovascular disease (CVD) remains the single largest cause of morbidity and mortality. As a result, accurate prediction of CVD risk is a component of medical care that has the potential to focus and direct preventative and diagnostic activities. Current methods of risk prediction in use in general clinical care are not highly accurate and, as a result, there is a potential unmet need for improved risk prediction instruments.

Components of cardiovascular disease (CVD) risk include family history, cigarette smoking, hypertension, and lifestyle factors such as diet and exercise. Also, numerous laboratory tests have been associated with CVD risk, most prominently lipids such as low-density lipoprotein (LDL) and high-density lipoprotein (HDL). These clinical and lipid factors are often combined into simple risk prediction instruments, such as Framingham Risk Score. The Framingham Risk Score provides an estimate of the 10-year risk for developing cardiac disease and is currently used in clinical care to determine the aggressiveness of risk factor intervention, such as the decision to treat hyperlipidemia with statins.

Many additional biomarkers, genetic factors and radiologic measures have been associated with increased risk of CVD. These include:

- Lipid markers: In addition to LDL and HDL, other lipid markers that may have predictive ability, including apolipoproteins, lipoprotein (a) (Lp[a]), and lipid subfractions
- Inflammatory markers: Many measures of inflammation have been linked to the likelihood of CVD. High-sensitivity C-reactive protein (hs-CRP) is an example of an inflammatory markers; others include fibrinogen, interleukins, and tumor necrosis factor. Increased CRP may reflect plaque instability and an increased risk for a CVD event.
- Metabolic syndrome biomarkers: Measures associated with metabolic syndrome, such as specific dyslipidemic profiles of serum insulin levels, have been associated with increased risk of CVD.
- Genetic Markers (genomic profiling): A number of variants associated with increased thrombosis risk, such as the MTHFR variant of the prothrombin gene variants, have been associated with increased CVD risk.

C. Definitions

- **Biomarker** - A distinctive biological or biologically derived indicator (as a biochemical metabolite in the body) of a process, event, or condition (as aging, disease, or exposure to a toxic substance).
- **Framingham Risk Score -** The Framingham Risk Score is a gender-specific algorithm used to estimate the 10-year cardiovascular risk of an individual. The Framingham Risk Score was first developed based on data obtained from the

Framingham Heart Study, to estimate the 10-year risk of developing coronary heart disease

- **Lipid Profile or Panel -** A lipid profile or lipid panel is a panel of blood tests that serves as an initial broad medical screening tool for abnormalities in lipids, such as cholesterol and triglycerides.
- **Risk Calculator -** A tool to help clinicians evaluate the 10 year and lifetime risks for CVD. It is an equation based on information such as race, gender, age, cholesterol, blood pressure, diabetes status, smoking status, and use of blood pressure medication. Examples of risk calculators can be found in the 2013 ACC/AHA Guideline on the Assessment of Cardiovascular Risk.
- **Risk factors -** Something that increases risk or susceptibility of CVD. (for example, hypertension, cigarette smoking, diabetes mellitus, premature family history of CVD, chronic kidney disease and obesity).

D. Policy

I. High-Sensitivity C-Reactive Protein (hs-CRP)

CareSource considers high-sensitivity C-reactive protein (hs-CRP) testing medically necessary for members who meet all of the criteria listed below:

A. The member has 2 or more coronary heart disease (CHD) major risk factors
B. The member has low-density lipoprotein (LDL) cholesterol levels between 100 to 130 mg/dL
C. When the hsCRP would add substantial incremental information in the decision making process to optimize/maximize lipid lowering pharmacologic therapy, (e.g., use of statins), in a member has been judged to be at an intermediate-risk of cardiovascular disease by global risk assessment (i.e., 10 to 20 %risk of CHD per 10 years using Framingham point scoring)
D. Major risk factors include:
    1. Age (men aged 45 years or older; women aged 55 years or older)
    2. Current cigarette smoking
    3. Family history of premature CHD (CHD in male first-degree relative less than 55 years of age; CHD in female first-degree relative less than 65 years of age)
    4. Hypertension (blood pressure [BP] of 140 mm Hg or higher, or on anti-hypertensive medication)
    5. Low high-density lipoprotein (HDL) cholesterol (less than 40mg/dL).
E. CareSource should only reimburse CPT code 86141, which represents high sensitivity C-reactive protein (hsCRP) testing once per year.

NOTE: CareSource considers hs-CRP testing experimental and investigational for all other indications, including use as a screening test for the general population and for monitoring response to therapy, because its clinical value for these uses has not been established.

II. Apolipoprotein B (apo B)

CareSource considers measurement of apolipoprotein B (apoB) medically necessary for use in high-risk members with hypercholesterolemia to assess whether additional intense interventions are necessary when LDL cholesterol goals are reached (LDL

cholesterol less than 70 mg/dL and non-HDL cholesterol less than 100 mg/dL in persons with known cardio-vascular disease (CVD) or diabetes mellitus, or LDL-C less than100 mg/dL and non-HDL cholesterol less than 130 mg/dL in persons with other risk factors). High-risk members are those with 1 or more of the following criteria:

A. Diabetes mellitus;
B. Known CVD; or
C. Two or more of the following CVD risk factors:
    1. Current cigarette smoking;
    2. Family history of premature CVD (CHD in male first-degree relative less than 55 years of age; CHD in female first-degree relative less than 65 years of age);
    3. Hypertension (BP of 140 mm Hg or higher, or on anti-hypertensive medication).

NOTE: CareSource considers measurement of apolipoprotein B (apoB) experimental and investigational for all other indications because its clinical value for other indications has not been established.

III. CV Risk Testing

While they may be appropriate for other indications, the medical literature does not support the utility of the following tests/devices for screening, diagnosis, or management of CVD:

- Activated factor VII
- Adiponectin
- Angiotensin gene (CardiaRisk AGT)
- Anti-thrombin III
- Apelin
- Apolipoprotein A-I (apo AI) (Boston Heart HDL Map panel)
- Apolipoprotein E (apo E)
- Apolipopritein E genotyping
- ASCVD risk testing (individual or panel) (eg, c-peptide, islet cell antibodies, nonesterified fatty acids (free fatty acids), proinsulin and total insulin)
- B-type natriuretic peptides
- CADence System
- Carotid ultrasound screening of asymptomatic persons for carotid artery stenosis
- Cathepsin S
- Chromosome 9 polymorphism 9p21
- Circulating microRNAs (e.g., miR-1, miR-16, miR-26a, miR-27a, andmiR-29a, miR-133a, and miR-199a-5p; not an all-inclusive list)
- Coenzyme Q10 (CoQ10)
- Coronary artery reactivity test
- Corus CAD Gene Expression Profile
- Cystatin-C
- Endothelin testing
- Factor II (thrombin) (F2 gene)

- Factor V Leiden (F5 gene)
- Fibrinogen
- 4q25 genotype testing (e g, 4q25-AF Risk Genotype Test, Cardio IQ4q25-AF Risk Genotype Test)
- Galectin-3
- Genetic testing (for genetic testing for familial hypercholesterolemia
- GlycA (glycosylated acute phase proteins)
- Growth stimulation expressed gene 2 (ST2)
- HDL subspecies (LpAI, LpAI/AII and/or HDL3 and HDL2
- Homocysteine testing
- Interleukin 6 (IL-6)
- Interleukin 6 -174 g/c promoter polymorphism
- AG.Interleukin 17 gene polymorphism
- Interleukin 18 (IL-18)
- Kinesin-like protein 6 (KLP6)
- LDL gradient gel electrophoresis
- LDL subspecies (small and large LDL particles)
- Leptin
- Lipidomic and metabolomic risk markers
- Lipoprotein remnants: intermediate density lipoproteins (IDL) and small density lipoproteins
- Lipoprotein(a) (Lp(a)) enzyme immunoassay
- Lipoprotein-associated phospholipase A2 (Lp-PLA2) (PLAC)
- Long chain omega-3 fatty acids composition in red blood cell
- LPA Intron-25 genotype testing (eg, Cardio IQ Intron-25 GenotypeTest, LPA Intron-25 Genotype Test)
- MaxPulse testing
- Measurement of free fatty acids
- Methods to determine vascular age
- Mid-regional pro-atrial natriuretic peptide
- MIRISK VP test
- MTHFR genetic testing
- Myeloperoxidase (MPO)
- Natriuretic peptide
- NMR Lipoprofile
- Osteoprotegerin
- Oxidized phospholipids
- Peroxisome proliferator-activated receptor
- Plasma ceramide
- Plasminogen activator inhibitor (PAI–1)
- Pregnancy-associated plasma protein-A (PAPP-A)
- Protein C
- Prothrombin gene mutation testing
- QuantaFlo System for evaluation of peripheral arterial disease

- Receptor for advanced glycosylation end products (RAGE) geneGly82Ser polymorphism testing
- Resistin
- Retinol binding protein 4 (RBP4)
- Serum sterols (eg, Boston Heart Cholesterol Balance Test)
- Singulex SMC testing for risk of cardiac dysfunction and vascular inflammation (eg, SMC Endothelin, SMC IL-6, SMC IL 17A, SMC c TnI and SMC TNF-α)
- Skin cholesterol (eg, PREVU)
- SLCO1B1 (statin induced myopathy genetic testing)
- SNP-based testing (eg, Cardiac Healthy Weight DNA Insight, Healthy Woman DNA Insight Test, Heart Health Genetic Test)
- Soluble cell adhesion molecules (e.g., intercellular adhesionmolecule-1 [ICAM-1], vascular cell adhesion molecule-1 [VCAM-1], E-selectin, and P-selectin)
- Thromboxane metabolite(s) testing
- Tissue plasminogen activator (tPA)
- Toll-like receptor 4 (TLR4) Asp299Gly (rs4986790) polymorphism
- Transforming growth factor beta
- Troponin I (eg, PATHFAST cTnI-II)
- Tumor necrosis factor-alpha (TNF-a)
- Total cholesterol content in red blood cell membranes
- Vertical Auto Profile (VAP) with or without vertical lipoprotein particle (VLP) technology
- Visfatin
- von Willebrand factor antigen level.

E. Conditions of Coverage

F. Related Policies/Rules

Lipid Testing in Assessing Risk for Cardiovascular Disease (CVD) MM-0012.

G. Review/Revision History

	DATE	ACTION
Date Issued	01/20/2021	New Policy
Date Revised		
Date Effective		
Date Archived	06/30/2021	This Policy is no longer active and has been archived. Please note that there could be other Policies that may have some of the same rules incorporated and CareSource reserves the right to follow CMS/State/NCCI guidelines without a formal documented Policy.

H. References

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Himmelfarb CD, Khera A, Lloyd-Jones D, McEvoy JW, Michos ED, Miedema MD, Muñoz D, Smith SC Jr, Virani SS, Williams KA Sr, Yeboah J, Ziaeian B. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2019;000: DOI: 10.1161/CIR.0000000000000678

2. Ballantyne CM, Hoogeveen RC, Bang H, et al. Lipoprotein-associated phospholipase A2, high-sensitivity C-reactive protein, and risk for incident coronary heart disease in middle-aged men and women in the Atherosclerosis Risk in Communities (ARIC) study. Circulation.2004;109(7):837-842.
3. Boekholdt SM, Arsenault BJ, Mora S, et al. Association of LDL cholesterol, non-HDL cholesterol, and apolipoprotein B levels with risk of cardiovascular events among patients treated with statins. A meta-analysis. JAMA. 2012;307(12):1302-1309.
4. Emerging Risk Factors Collaboration, Kaptoge S, Di Angelantonio E, Pennells L, et al. C-reactive protein, fibrinogen, and cardiovascular disease prediction. N Engl J Med. 2012;367(14):1310-1320.
5. Yeh ET. High-sensitivity C-reactive protein as a risk assessment tool for cardiovascular disease. Clin Cardiol. 2005;28(9):408-412.

The Medical Policy Statement detailed above has received due consideration as defined in the Medical Policy Statement Policy and is approved.