Scott&White HEALTH PLAN
PART OF BAYLOR SCOTT & WHITE HEALTH

MEDICAL COVERAGE POLICY

SERVICE:	**Apolipoprotein E Genotype or Phenotype in the Management of Cardiovascular Disease**
Policy Number:	**014**
Effective Date:	**12/01/2019**
Last Review:	**09/26/2019**
Next Review Date:	**09/26/2020**

Important note:
Unless otherwise indicated, this policy will apply to all lines of business.
Even though this policy may indicate that a particular service or supply may be considered medically necessary and thus covered, this conclusion is not based upon the terms of your particular benefit plan. Each benefit plan contains its own specific provisions for coverage and exclusions. Not all benefits that are determined to be medically necessary will be covered benefits under the terms of your benefit plan. You need to consult the Evidence of Coverage (EOC) or Summary Plan Description (SPD) to determine if there are any exclusions or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and your plan of benefits, the provisions of your benefits plan will govern. However, applicable state mandates will take precedence with respect to fully insured plans and self-funded non-ERISA (e.g., government, school boards, church) plans. Unless otherwise specifically excluded, Federal mandates will apply to all plans. With respect to Medicare-linked plan members, this policy will apply unless there are Medicare policies that provide differing coverage rules, in which case Medicare coverage rules supersede guidelines in this policy. Medicare-linked plan policies will only apply to benefits paid for under Medicare rules, and not to any other health benefit plan benefits. CMS's Coverage Issues Manual can be found on the CMS website. Similarly, for Medicaid-linked plans, the Texas Medicaid Provider Procedures Manual (TMPPM) supersedes coverage guidelines in this policy where applicable.

SERVICE: Apolipoprotein E Genotype or Phenotype in the Management of Cardiovascular Disease

PRIOR AUTHORIZATION: Not applicable.

POLICY: SWHP considers Apolipoprotein E Genotype or Phenotype Testing in the management of cardiovascular disease to be unproven and not medically necessary**.**

OVERVIEW: Apolipoprotein E (apo E) is the primary apolipoprotein found in very-low-density lipoproteins (VLDLs) and chylomicrons. Apo E is the primary binding protein for low density lipoproteins (LDL) receptors in the liver and is thought to play an important role in lipid metabolism. The apo E gene is polymorphic, consisting of three alleles (e2, e3, and e4) that code for 3 protein isoforms, known as E2, E3, and E4, which differ from one another by one amino acid. These molecules mediate lipid metabolism through their different interactions with the LDL receptors. The genotype of apo E alleles can be assessed by gene amplification techniques, while the apo E phenotype can be assessed by measuring plasma levels of apolipoprotein E.

There is some evidence that apo E isoforms have different effects on serum cholesterol and triglyceride (TG) levels and may influence risk of developing cardiovascular disease (CVD). However, the effect of the apo E isoform types on lipid metabolism and development of atherosclerosis is complex and incompletely understood, and, to date, there has been no health benefit associated with apo E testing. At the present time, there is no evidence to support the use of apo E testing, using either genetic or protein methods, for the screening, diagnosis, or management of dyslipidemia and/or CVD.that indicates diminished response. None of the available evidence provides adequate data to establish that apo E genotype or phenotype improves outcomes when used in clinical care.

The American Association of Clinical Chemistry (AACC, 2009) has stated that the test for apo E is not widely used and its clinical usefulness is still being researched. Furthermore, available evidence indicates that apo E genotype is a poor predictor of ischemic stroke.

CODES:
Important note:

Scott&White HEALTH PLAN
PART OF BAYLOR SCOTT & WHITE HEALTH

MEDICAL COVERAGE POLICY

SERVICE:	**Apolipoprotein E Genotype or Phenotype in the Management of Cardiovascular Disease**
Policy Number:	**014**
Effective Date:	**12/01/2019**
Last Review:	**09/26/2019**
Next Review Date:	**09/26/2020**

CODES: Due to the wide range of applicable diagnosis codes and potential changes to codes, an inclusive list may not be presented, but the following codes may apply. Inclusion of a code in this section does not guarantee that it will be reimbursed, and patient must meet the criteria set forth in the policy language.

CPT Not Covered:	82172

CMS: There are no NCDs or LCDs.

POLICY HISTORY:

Status	Date	Action
New	12/3/2010	New policy
Reviewed	12/2/2011	Reviewed.
Reviewed	10/25/2012	Reviewed.
Reviewed	10/3/2013	No changes
Reviewed	06/19/2014	No changes
Reviewed	07/02/2015	No changes
Reviewed	07/28/2016	No changes
Reviewed	06/19/2018	Updated language and references
Reviewed	09/26/2019	No changes

REFERENCES:

The following scientific references were utilized in the formulation of this medical policy. SWHP will continue to review clinical evidence related to this policy and may modify it at a later date based upon the evolution of the published clinical evidence. Should additional scientific studies become available and they are not included in the list, please forward the reference(s) to SWHP so the information can be reviewed by the Medical Coverage Policy Committee (MCPC) and the Quality Improvement Committee (QIC) to determine if a modification of the policy is in order.

1. Eichner JE, Dunn ST, Perveen G et al. Apolipoprotein E polymorphism and cardiovascular disease: a HuGE review. Am J Epidemiol 2002; 155(6):487-95.
2. Ordovas JM, Mooser V. The APOE locus and the pharmacogenetics of lipid response. Curr Opin Lipidol 2002; 13(2):113-7.
3. Snow V, Aronson MD, Hornbake ER et al. Lipid control in the management of type 2
4. diabetes mellitus: a Clinical Practice Guideline from the American College of Physicians. Ann Intern Med 2004; 140(8):644-9.
5. Volcik KA, Barkley RA, Hutchinson RG et al. Apolipoprotein E polymorphisms predict low density lipoprotein levels and carotid artery wall thickness but not incident coronary heart disease in 1,491 ARIC study participants. Am J Epidemiol 2006; 164(4):342-8.
6. Eiriksdottir G, Aspelund T, Bjarnadottir K et al. Apolipoprotein E genotype and statins affect CRP levels through independent and different mechanisms: AGES-Reykjavik Study. Atherosclerosis 2006; 186(1):222-
7. Tziakas DN, Chalikias GK, Antonoglou CO et al. Apolipoprotein E genotype and circulating interleukin-10 levels in patients with stable and unstable coronary artery disease. J Am Coll Cardiol 2006; 48(12):2471-81.
8. Vaisi-Raygani A, Rahimi Z, Nomani H et al. The presence of apolipoprotein epsilon4 and epsilon2 alleles augments the risk of coronary artery disease in type 2 diabetic patients. Clin Biochem 2007; 40(15):1150-6.
9. Bennet AM, Di Angelantonio E, Ye Z et al. Association of apolipoprotein E genotypes with lipid levels and coronary risk. JAMA 2007; 298(11):1300-11.
10. Schmitz F, Mevissen V, Krantz C et al. Robust association of the APOE epsilon4 allele with premature myocardial infarction especially in patients without hypercholesterolemia. Eur J Clin Invest 2007; 37(2):106-8.

11. Chiodini BD, Franzosi MG, Barlera S et al. Apolipoprotein E polymorphisms influence effect of pravastatin on survival after myocardial infarction in a Mediterranean population. Eur Heart J 2007; 28(16):1977-83.
12. Koch W, Hoppmann P, Schomig A et al. Apolipoprotein E gene epsilon2/epsilon3/epsilon4 polymorphism and myocardial infarction: case-control study in a large population sample. Int J Cardiol 2008; 125(1):116-7.
13. Kulminski AM, Ukraintseva SV, Arbeev KG et al. Health-protective and adverse effects of the apolipoprotein E epsilon2 allele in older men. J Am Geriatr Soc 2008; 56(3):478- 83.
14. Apolipoprotein E Genotype or Phenotype in the Management of Cardiovascular Disease.
15. Donnelly LA, Palmer CN, Whitley AL et al. Apolipoprotein E genotypes are associated with lipid-lowering responses to statin treatment in diabetes: a Go-DARTS study. Pharmacogenet Genomics 2008; 18(4):279-87.
16. Vossen CY, Hoffmann MM, Hahmann H et al. Effect of Apo E genotype on lipid levels in patients with coronary heart disease during a 3-week inpatient rehabilitation program. Clin Pharmacol Ther 2008; 84(2):222-7.
17. Novel Lipid Risk Factors In Risk Assessment and Management of Cardiovascular Disease. Chicago, Illinois: Blue Cross Blue Shield Association Medical Policy Reference Manual (2010 June). Medicine 2.04.25.
18. Contois JH, McConnell JP, Sethi AA, et al.; AACC Lipoproteins and Vascular Diseases Division Working Group on Best Practices. Apolipoprotein B and cardiovascular disease risk: Position statement from the AACC Lipoproteins and Vascular Diseases Division Working Group on Best Practices. Clin Chem. 2009;55(3):407-419.