Department:	Medical Management	**Original Approval:**	10/18/2017
Policy #:	MM160	**Last Approval:**	02/01/2019
Title:	MTHFR Polymorphism Genetic Testing		
Approved By:	Utilization Management Committee		

REQUIRED DOCUMENTATION

Clinical documentation including history, exam, laboratory testing, assessment, and plan, explanation of expected benefit of the requested testing and how it will impact care of the member.

BACKGROUND

Methylenetetrahydrofolate Reductase (MTHFR) enzyme plays an important role in processing amino acids, specifically, the conversion of homocysteine to methionine and is encoded by the MTHFR gene. In the US, 35 percent of the population has one copy of the C677T MTHFR allele, and 10-15 percent of the population has two copies of the C677T MTHFR allele. This makes it a common polymorphism, not a disease-causing mutation.

The American College of Medical Genetics (ACMG):
"MTHFR polymorphism testing is frequently ordered by physicians as part of the clinical evaluation for thrombophilia. It was previously hypothesized that reduced enzyme activity of MTHFR led to mild hyperhomocysteinemia which led to an increased risk for venous thromboembolism, coronary heart disease, and recurrent pregnancy loss. Recent meta-analyses have disproven an association between hyperhomocysteinemia and risk for coronary heart disease and between MTHFR polymorphism status and risk for venous thromboembolism. There is growing evidence that MTHFR polymorphism testing has minimal clinical utility and, therefore should not be ordered as a part of a routine evaluation for thrombophilia."

The ACMG practice guidelines on genetic testing for MTHFR state:

- MTHFR polymorphism genotyping should not be ordered for at risk family members.
- MTHFR polymorphism genotyping should not be ordered as part of the clinical evaluation for thrombophilia or recurrent pregnancy loss.
- There is currently no evidence that specific treatments reduce risks associated with homocysteinemia or MTHFR genotype status.
- MTHFR status does not change the recommendation that women of childbearing age should take the standard dose of folic acid supplementation to reduce the risk of neural tube defects as per the general population guidelines.

References:

Genet Med advance online publication 3 January 2013 and American College of Medical Genetics and Genomics (ACMG) Practice Guideline: lack of evidence for MTHFR polymorphism testing, Scott E. Hickey, et al. January 2013
https://www.acmg.net/StaticContent/PPG/MTHFT_pre-print.pdf
https://www.acmg.net/docs/MTHFR_gim2012165a_Feb2013.pdf

DEFINITIONS

None.

INDICATIONS/CRITERIA

For Apple Health Members:

According to the HCA policy on Pharmacogenomic testing (20170120A, Pharmacogenomic testing for selected conditions):
Pharmacogenomic testing for is not covered for the following conditions:

- depression
- mood disorders
- psychosis
- anxiety
- ADHD
- substance use disorder

https://www.hca.wa.gov/assets/program/PDX-final-findings-decision-20170317.pdf
For other conditions, coverage is subject to evaluation of medical necessity.

SPECIAL CONSIDERATIONS

For Medicare Members:
MTHFR testing is not covered.
"Finally, despite many earlier publications suggesting a link between MTHFR polymorphisms and a risk for a wide spectrum of obstetric and cardiovascular complications, it is now accepted that MTHFR genotype alone is not associated with VTE. There is no clinical indication for MTHFR genotyping in any population.

There is broad consensus in the medical literature that MTHFR genotyping has no clinical utility in any clinical scenario. This testing is considered investigational and is NOT a Medicare benefit."
See LCD: GENETIC TESTING for Hypercoagulability / Thrombophilia (Factor V Leiden, Factor II Prothrombin, and MTHFR) (L36159)

LIMITATIONS/EXCLUSIONS

Please refer to a product line's certificate of coverage for benefit limitations and exclusions for these services:

PRODUCT LINE	LINK TO CERTIFICATE OF COVERAGE
MEDICARE ADVANTAGE	http://healthfirst.chpw.org/for-members/resource-library/handbooks-and-guides
WASHINGTON HEALTH PROGRAM	http://chpw.org/our-plans/apple-health/

Citations & References

CFR		
WAC		
RCW		
Contract Citation	☒ WAH	11.2.9
	☒ IMC	
	☒ MA	
Other Requirements		
NCQA Elements		

Revision History

Revision Date	Revision Description	Revision Made By
10/16/2017	Policy Creation	LuAnn Chen, MD
10/17/2017	Formatted to CCC Template	Sheila Ranganathan, RN
10/17/2017	Re-Formatted	Cyndi Stilson, RN
10/18/2017	Approval	MMLT
03/21/2018	Updated background, indications and special consideration sections	LuAnn Chen, MD
03/21/2018	Approval	UM Committee
01/28/2019	Added required documentation, as per WAC.	LuAnn Chen, MD
02/01/2019	Approval	UM Committee