Genetic Testing for Methylene Tetrahydrofolate Reductase

Humana

Effective Date: 03/28/2024 Revision Date: 03/28/2024 Review Date: 03/28/2024 Policy Number: HUM-0543-009 Line of Business: Commercial

Medical Coverage Policy

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Related Medical/Pharmacy Coverage Policies

None

Description

The methylene tetrahydrofolate reductase (MTHFR) enzyme is encoded by the *MTHFR* gene. This enzyme plays a role in processing amino acids (the building blocks of proteins) which is important for a chemical reaction involving forms of the vitamin folate and is required for the multistep process that converts the amino acid homocysteine to another amino acid, methionine. The body uses methionine to make proteins and other important compounds.

Variations in the *MTHFR* gene have been studied as risk factors for numerous conditions, including behavioral disorders, cardiovascular disease, thrombophilia, stroke, hypertension, pharmacological management or risk testing and pregnancy-related complications; however, its role remains unclear.

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Humana recognizes that the field of genetic testing is rapidly changing and that other tests may become available.

Coverage Determination

Any state mandates for genetic testing for *MTHFR* take precedence over this medical coverage policy.

Genetic testing may be excluded by certificate. Please consult the member's individual certificate regarding Plan coverage.

Humana members may **NOT** be eligible under the Plan for **genetic testing for** *MTHFR* **(81291)**, **individually or as part of a panel**. This is considered experimental/ investigational as it is not identified as widely used and generally accepted for the proposed use as reported in nationally recognized peer-reviewed medical literature published in the English language.

Coding Information

Any codes listed on this policy are for informational purposes only. Do not rely on the accuracy and inclusion of specific codes. Inclusion of a code does not guarantee coverage and/or reimbursement for a service or procedure.

CPT® Code(s)	Description	Comments
81291	MTHFR (5,10-methylenetetrahydrofolate reductase) (eg, hereditary hypercoagulability) gene analysis, common variants (eg, 677T, 1298C)	Not Covered
CPT®		
Category III Code(s)	Description	Comments
No code(s) identified		
HCPCS	Description	Comments
Code(s)		
No code(s) identified		

References

- American College of Medical Genetics and Genomics (ACMG). ACMG Practice Guidelines. Lack of evidence for *MTHFR* polymorphism testing. <u>https://www.acmg.net</u>. Published February 2013. Updated April 27, 2020.
- 2. American College of Obstetricians and Gynecologists (ACOG). Practice Bulletin. Inherited thrombophilias in pregnancy. <u>https://www.acog.org</u>. Published September 2013. Updated July 2022.

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- 3. American College of Obstetricians and Gynecologists (ACOG). Practice Bulletin. Neural tube defects. https://www.acog.org. Published December 2017. Updated 2021.
- 4. American Heart Association (AHA). AHA Science Advisory. Homocyst(e)ine, diet, and cardiovascular diseases: a statement for healthcare professionals from the Nutrition Committee, American Heart Association. <u>https://www.americanheart.org</u>. Published January 12, 1999.
- Clinical Genome Resource (ClinGen). Gene-Disease Validity Classification Summary. MTHFR homocystinuria due to methylene tetrahydrofolate reductase deficiency. <u>https://www.clinicalgenome.org</u>. Published June 18, 2019.
- 6. Clinical Pharmacogenetics Implementation Consortium (CPIC). CPIC gene-drugs for MTHFR. <u>https://www.cpic.com.</u> Published June 1, 2022.
- 7. ECRI Institute. ECRIgene Genetic Test Assessment. GeneSight MTHFR (Assurex Health, Inc.) for aiding diagnosis of hyperhomocysteniemia and guiding selection and dosage of folic acid supplements. <u>https://www.ecri.org</u>. Published September 2019.
- 8. Hayes, Inc. Clinical Utility Evaluation. *MTHFR* genetic testing for hypertension. <u>https://evidence.hayesinc.com</u>. Published December 22, 2023.
- 9. Hayes, Inc. Clinical Utility Evaluation. *MTHFR* genetic testing for nondevelopmental psychiatric disorders. <u>https://evidence.hayesinc.com</u>. Published December 12, 2023.
- 10. Hayes, Inc. Clinical Utility Evaluation. *MTHFR* genetic testing for pregnancy complications. <u>https://evidence.hayesinc.com</u>. Published November 28, 2023.
- 11. Hayes, Inc. Clinical Utility Evaluation. *MTHFR* genetic testing for severe *MTHFR* enzyme deficiency. <u>https://evidence.hayesinc.com</u>. Published August 17, 2017. Updated September 29, 2023.
- 12. Hayes, Inc. Clinical Utility Evaluation. *MTHFR* pharmacogenomic genotyping for altering drug treatments. <u>https://evidence.hayesinc.com</u>. Published March 23, 2017. Updated May 23, 2021.
- 13. Hayes, Inc. Precision Medicine Research Brief. *MTHFR* pharmacogenomic genotyping for altering drug treatments. <u>https://evidence.hayesinc.com</u>. Published August 1, 2023.
- 14. MCG Health. Hyperhomocysteinemia *MTHFR* gene. 27th edition. https://humana.access.mcg.com/index
- 15. MCG Health. Methotrexate pharmacogenetics *MTHFR* gene. 27th edition. <u>https://humana.access.mcg.com/index</u>
- 16. National Center for Biotechnology Information (NCBI). Genetic Testing Registry (GTR). Prothrombin thrombophilia. <u>https://www.ncbi.nlm.nih.gov/gtr</u>. Published July 25, 2006. Updated February 4, 2021.

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- National Society of Genetic Counselors (NSGC). Genetic evaluation and counseling of couples with recurrent miscarriage: recommendations of the National Society of Genetic Counselors. <u>https://nsgc.org</u>. Published June 2005.
- 18. UpToDate, Inc. Causes and pathophysiology of vitamin B12 and folate deficiencies. https://www.uptodate.com. Updated January 2024.
- 19. UpToDate, Inc. Evaluating patients with established venous thromboembolism for acquired and inherited risk factors. <u>https://www.uptodate.com</u>. Updated January 2024.
- 20. UpToDate, Inc. Inherited thrombophilias in pregnancy. <u>https://www.uptodate.com</u>. Updated January 2024.
- 21. UpToDate, Inc. Hereditary thrombophilia testing in adults without VTE. <u>https://www.uptodate.com</u>. Updated February 2024.
- 22. UpToDate, Inc. Neural tube defects: overview of prenatal screening, evaluation and pregnancy management. <u>https://www.uptodate.com</u>. Updated January 2024.
- 23. UpToDate, Inc. Overview of homocysteine. <u>https://www.uptodate.com</u>. Updated January 2024.
- 24. UpToDate, Inc. Overview of the causes of venous thrombosis. <u>https://www.uptodate.com</u>. Updated January 2024.
- 25. UpToDate, Inc. Thrombophilia testing in children and adolescents. <u>https://www.uptodate.com</u>. Updated January 2024.

Change Summary

- 03/28/2024 Annual Review, No Coverage Change.