Medica Central Coverage Policy

Policy Name: Genetic Testing - Specialty Testing: Nutrition and Metabolism

Effective Date: 07/01/2025

Important Information – Please Read Before Using This Policy

These services may or may not be covered by all Medica Central plans. Coverage is subject to requirements in applicable federal or state laws. Please refer to the member's plan document for other specific coverage information. If there is a difference between this general information and the member's plan document, the member's plan document will be used to determine coverage. With respect to Medicare, Medicaid, and other government programs, this policy will apply unless these programs require different coverage.

Members may contact Medica Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions may call the Provider Service Center. Please use the Quick Reference Guide on the Provider Communications page for the appropriate phone number. https://mo-central.medica.com/Providers/SSM-employee-health-plan-for-IL-MO-OK-providers

Medica Central coverage policies are not medical advice. Members should consult with appropriate health care providers to obtain needed medical advice, care, and treatment.

OVERVIEW

This policy addresses the use of tests for nutrition and metabolism.

For additional information see the Rationale and References section.

The tests, CPT codes, and ICD codes referenced in this policy are not comprehensive, and their inclusion does not represent a guarantee of coverage or non-coverage.

POLICY REFERENCE TABLE

COVERAGE CRITERIA SECTIONS	EXAMPLE TESTS (LABS)	COMMON BILLING CODES	SUPPORT
Methylenetetrahydrofolate Reductase (MTHFR) Deficiency			
MTHFR Variant Analysis	Methylenetetrahydrofolate Reductase (MTHFR) Thermolabile Variant, DNA Analysis (LabCorp)	81291, E03.9, E55.9, E72.12, E78.2, E78.5, E88.9, N96, O03, R53.83, Z00.00	Rationale/ References
	Methylenetetrahydrofolate Reductase (MTHFR), DNA Mutation Analysis (Quest Diagnostics)		
Other Covered Metabolic Disorders			

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COVERAGE CRITERIA SECTIONS	EXAMPLE TESTS (LABS)	COMMON BILLING CODES	SUPPORT
Other Covered Metabolic Disorders	See list below	81400, 81401, 81402, 81403, 81404, 81405, 81406, 81407, 81408, 81250	Additional References

RELATED POLICIES

This policy document provides coverage criteria for nutrition and metabolism. Please refer to:

- ***Specialty Testing: Multisystem Genetic Conditions*** for coverage criteria related to diagnostic tests for genetic disorders that affect multiple organ systems (e.g. whole exome and genome sequencing, chromosomal microarray, and multigene panels for broad phenotypes).
- ***General Approach to Laboratory Testing*** for coverage criteria related to nutrition and metabolism, including known familial variant testing, that is not specifically discussed in this or another non-general policy.

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COVERAGE CRITERIA

METHYLENETETRAHYDROFOLATE REDUCTASE (MTHFR) DEFICIENCY

MTHFR Variant Analysis

I. *MTHFR* targeted variant analysis (e.g., 677T, 1298C) is considered **investigational** for all indications, including but not limited to:

   A. Evaluation for thrombophilia or recurrent pregnancy loss

   B. Evaluation of at-risk relatives

   C. Drug metabolism, such as in pharmacogenetic testing.

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OTHER COVERED METABOLIC DISORDERS

Other Covered Metabolic Disorders

The following is a list of conditions that have a known genetic association. Due to their relative rareness, it may be appropriate to cover these genetic tests to establish or confirm a diagnosis.

I. Genetic testing to establish or confirm one of the following metabolic conditions to guide management is considered **medically necessary** when the member demonstrates clinical features consistent with the disorder (the list is not meant to be comprehensive, see II below):

   A. Congenital adrenal hyperplasia, including:

1. 21-Hydroxylase deficiency

B. Congenital disorders of glycosylation

C. Congenital hyperinsulinism

D. Disorders of amino acid and peptide metabolism, including:

1. Glutaric acidemia type I (GA-1)
2. Homocystinuria caused by cystathionine beta-synthase (CBS) deficiency
3. Methylmalonic acidemia
4. Propionic acidemia
5. Maple Syrup Urine Disease (MSUD)

E. Disorders of biotin metabolism, including:

1. Biotinidase deficiency

F. Disorders of carnitine transport and the carnitine cycle, including:

1. Carnitine palmitoyltransferase II deficiency
2. Primary carnitine deficiency

G. Disorders of copper metabolism, including:

1. ATP7A-Related copper transport disorders (e.g., Menkes disease, occipital horn syndrome (OHS), ATP7A-related distal motor neuropathies)
2. Wilson disease

H. Disorders of fatty acid oxidation, including:

1. Medium-chain acyl-coenzyme A dehydrogenase deficiency (MCAD deficiency)

I. Disorders of galactose metabolism, including:

1. Galactosemia

J. Disorders of glucose transport, including:

1. Glucose transporter type I deficiency syndrome (Glut1 DS)

K. Disorders of phenylalanine or tyrosine metabolism, including:

1. Alkaptonuria
2. Phenylalanine hydroxylase deficiency

L. Disorders of porphyrin and heme metabolism, including:

1. Acute intermittent porphyria

M. Fibrous Dysplasia/McCune-Albright Syndrome

N. Glycogen storage disorders, including:

1. Glycogen Storage Disease Type I (GSDI)
2. Pompe disease (GSDII)

O. Hypophosphatasia

P. Kallmann syndrome (GnRH deficiency)

Q. Lysosomal storage disorders, including:

1. Gaucher disease
2. Krabbe disease
3. MPS-Type I (Hurler syndrome)
4. MPS-Type II (Hunter syndrome)
5. Mucolipidosis IV

R. Urea cycle disorders, including:

1. Ornithine Transcarbamylase (OTC) deficiency

S. Malignant hyperthermia

T. SHOX deficiency disorders.

II. Genetic testing to establish or confirm the diagnosis of all other metabolic disorders not specifically discussed within this or another medical policy will be evaluated by the criteria outlined in *General Approach to Laboratory Testing* (see policy for coverage criteria).

NOTE: Clinical features for a specific disorder may be outlined in resources such as GeneReviews, OMIM, National Library of Medicine, Genetics Home Reference, or other scholarly sources.

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PRIOR AUTHORIZATION

Prior authorization is not required. However, services with specific coverage criteria may be reviewed retrospectively to determine if criteria are being met. Retrospective denial may result if criteria are not met.

RATIONALE AND REFERENCES

MTHFR Variant Analysis
American College of Medical Genetics and Genomics (ACMG)

ACMG published a practice guideline, which they later reclassified as a clinical practice resource, for *MTHFR* polymorphism testing (2013, reaffirmed in 2020). The practice resource (called lack of evidence for MTHFR polymorphism testing) includes the following recommendations:

- *MTHFR* polymorphism genotyping should not be ordered as part of the clinical evaluation for thrombophilia or recurrent pregnancy loss
- *MTHFR* polymorphism genotyping should not be ordered for at-risk family members (p. 154).

Bashford MT, Hickey SE, Curry CJ, Toriello HV; American College of Medical Genetics and Genomics (ACMG) Professional Practice and Guidelines Committee. Addendum: ACMG Practice Guideline: lack of evidence for MTHFR polymorphism testing. Genet Med. 2020;22(12):2125. doi:10.1038/s41436-020-0843-0

American College of Obstetricians and Gynecologists (ACOG)

ACOG published practice bulletin No. 197 in 2018 (reaffirmed in 2022) called Inherited Thrombophilias in Pregnancy. ACOG does not include *MTHFR* mutation analysis in their list of recommended screening tests for inherited thrombophilias, and also points out a lack of association between *MTHFR* C677T polymorphisms and adverse pregnancy outcomes (p. e24 and e28). Additionally, ACOG notes that homozygosity for the *MTHFR* mutations themselves does not increase the risk for VTE in women (either pregnant or not pregnant) (p. e21).

American College of Obstetricians and Gynecologists' Committee on Practice Bulletins–Obstetrics. ACOG Practice Bulletin No. 197: Inherited Thrombophilias in Pregnancy [published correction appears in Obstet Gynecol. 2018 Oct;132(4):1069. (Reaffirmed 2022). Obstet Gynecol. 2018;132(1):e18-e34. doi:10.1097/AOG.0000000000002703 doi:10.1097/AOG.0000000000002924.]

Food and Drug Administration (FDA)

The FDA does not list *MTHFR* in Section 1 of the Table of Pharmacogenetic Associations ("Pharmacogenetic Associations for which the Data Support Therapeutic Management Recommendations").

Table of Pharmacogenetic Associations. FDA website. Updated October 26, 2022. https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations.

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ADDITIONAL REFERENCES

1. Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2025. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1116/
2. Online Mendelian Inheritance in Man, OMIM. McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University (Baltimore, MD). World Wide Web URL: https://omim.org/
3. MedlinePlus [Internet]. Bethesda (MD): National Library of Medicine (US). Available from: https://medlineplus.gov/genetics/.

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Note: The Health Plan uses the genetic testing clinical criteria developed by Concert Genetics, an industry-leader in genetic testing technology assessment and policy development.

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