Revision log
Coding Implications

CONCERT GENETIC TESTING: NUTRITION AND METABOLISM

OVERVIEW

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

For additional information see the Rationale section.

POLICY REFERENCE TABLE

Coding Implications

This clinical policy references Current Procedural Terminology (CPT®). CPT is a registered trademark of the American Medical Association. All CPT codes and descriptions are copyrighted 2024, American Medical Association. All rights reserved. CPT codes and CPT descriptions are from the current manuals and those included herein are not intended to be all-inclusive and are included for informational purposes only. Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

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. Please see the Concert Platform for additional registered tests.

CRITERIA SECTIONS	EXAMPLE TESTS (LABS)	COMMON BILLING CODES	REF
Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency			

G6PD Variant Analysis	G6PD Targeted Variant - Single Test (GeneDx) G6PD Full Gene Sequencing and Deletion/Duplication (Invitae)	81247, 81248, 81249, 81479, D55.0	1, 2
Methylenetetrahydrofolate Reductase (MTHFR) Deficiency			
MTHFR Variant Analysis	Methylenetetrahydrofolate Reductase (MTHFR) Thermolabile Variant, DNA Analysis (LabCorp) Methylenetetrahydrofolate Reductase (MTHFR), DNA Mutation Analysis (Quest Diagnostics)	81291, E03.9, E55.9, E72.12, E78.2, E78.5, E88.9, N96, O03, R53.83, Z00.00	3, 4
Other Covered Metabolic Disorders			
Other Covered Metabolic Disorders	See list below	81400, 81401, 81402, 81403, 81404, 81405, 81406, 81407, 81408, 81250	10, 11, 12, 29, 30

RELATED POLICIES

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

- ***Specialty Testing: Multisystem Genetic Conditions*** for 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 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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CRITERIA

It is the policy of health plans affiliated with Centene Corporation® that the specific genetic testing noted below is **medically necessary** when meeting the related criteria:

GLUCOSE-6-PHOSPHATE DEHYDROGENASE (G6PD) DEFICIENCY

G6PD Variant Analysis

I. Current evidence does not support *G6PD* variant analysis to confirm or establish a diagnosis of glucose-6-phosphate dehydrogenase deficiency for all indications.

NOTE: Diagnosis of *G6PD* deficiency can be achieved by quantitative spectrophotometric analysis or, more commonly, by a rapid fluorescent spot test detecting the generation of NADPH from NADP.

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METHYLENETETRAHYDROFOLATE REDUCTASE (MTHFR) DEFICIENCY

MTHFR Variant Analysis

I. Current evidence does not support *MTHFR* targeted variant analysis (e.g., 677T, 1298C) 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/enrollee 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 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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RATIONALE

G6PD Variant Analysis

American Academy of Family Physicians

Frank (2005) published guidelines in American Family Physician for evaluating individuals for *G6PD* deficiency, including specific laboratory tests which notably do not include genetic testing: "The diagnosis of *G6PD* deficiency is made by a quantitative spectrophotometric analysis or, more commonly, by a rapid fluorescent spot test detecting the generation of NADPH from NADP. The test is positive if the blood spot fails to fluoresce under ultraviolet light." (p. 1278).

UpToDate: Diagnosis and management of glucose-6-phosphate dehydrogenase (G6PD) deficiency

Per this summary of *G6PD* diagnosis and management, the tests commonly used are semi-quantitative screening tests, some of which are done at the point-of-care. Positive screening tests should be followed up with a quantitative test that reports G6PD enzyme activity per gram of hemoglobin. If initial results are negative, testing should be repeated three months following resolution of the hemolytic episode. Confirmatory testing using molecular methods (DNA) is available; however, it is not used routinely and is not useful for those of African or Mediterranean ancestry.

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MTHFR Variant Analysis

American College of Medical Genetics and Genomics (ACMG)

ACMG published a practice guideline for *MTHFR* polymorphism testing (2013, confirmed 2020) with 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).

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DEFINITIONS

1. **High myopia** is defined by the American Association for Pediatric Ophthalmology & Strabismus as near-sightedness of -6.00 diopters or greater or an axial length greater than 26.5mm.

2. **Marfanoid features**, or marfanoid habitus, refers to any of the features that typically are associated with Marfan Syndrome, including but not limited to disproportionately tall, slender build, abnormally long/slender fingers and toes, protruding or caving sternum,
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Reviews, Revisions, and Approvals	Revision Date	Approval Date
New policy created with criteria incorporated from other policies: G6PD Variant Analysis criteria incorporated from Concert Genetic Testing: Hematologic Conditions (Non-Cancerous); MTHFR Variant Analysis and Other Covered Metabolic Disorders criteria incorporated from MTHFR Variant Analysis. References, rationale, background and coding updated. "Investigational" policy statements changed to state that "current evidence does not support…"	11/25	12/25

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Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

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Note: For Medicaid member/enrollees, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare member/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs and LCDs and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.