Revision log
Coding Implications

CONCERT GENETIC TESTING: ENDOCRINOLOGY

See Important Reminder at the end of this policy for important regulatory and legal information.

OVERVIEW

This policy addresses the use of tests to measure various hormones and assess for diseases and conditions that primarily affect the endocrine system.

Pre-test and post-test genetic counseling that facilitates informed decision-making, addresses the possibility of secondary or incidental findings, and a plan for returning results before testing occurs is strongly advised.

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.

Monogenic Diabetes Panel Tests			
Monogenic Diabetes (Including Maturity Onset Diabetes of the Young (MODY)) Panels	Maturity Onset Diabetes of the Young (MODY) Panel (PreventionGenetics, part of Exact Sciences)	81403, 81405, 81406, 81407, 81479, E10, E11, E16.1, E16.2	1, 2, 5
	Maturity-onset diabetes of the young (MODY) (Ambry Genetics)		
	Monogenic Diabetes (MODY) Five Gene Evaluation (GCK,HNF1A,HNF1B,HNF4A,IPF1) (Athena Diagnostics Inc)		

RELATED POLICIES

This policy document provides criteria for endocrine disorders. Please refer to:

- ***General Approach to Laboratory Testing*** for criteria related to endocrine disorders not specifically discussed in this or another non-general policy, including known familial variant testing.

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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:

MONOGENIC DIABETES PANEL TESTS

Monogenic Diabetes (Including Maturity Onset Diabetes of the Young (MODY)) Panels

I. Multigene panel analysis to establish or confirm a diagnosis of monogenic diabetes (including maturity-onset diabetes of the young (MODY)) is considered **medically necessary** when:

   A. The member/enrollee has a diagnosis of diabetes within the first 12 months of life, **OR**

   B. The member/enrollee has a diagnosis of diabetes before 30 years of age, **AND**

      1. The member/enrollee has at least one of the following:

         a) Autoantibody negative, **OR**

         b) Retained C-peptide levels, **OR**

   C. The member/enrollee has a diagnosis of diabetes not characteristic of type 1 or type 2 diabetes, **AND**

      1. The member/enrollee has a family history of diabetes consistent with an autosomal dominant pattern of inheritance.

II. Current evidence does not support multigene panel analysis to establish or confirm a diagnosis of monogenic diabetes (maturity-onset diabetes of the young (MODY)) for all other indications.

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RATIONALE

Monogenic Diabetes (Including Maturity Onset Diabetes of the Young (MODY)) Panels

American Diabetes Association

In 2024, the American Diabetes Association made the following recommendations (p. S32):

- Individuals of any age who were diagnosed with diabetes in the first 6 months of life should have immediate genetic testing for neonatal diabetes (Category A).
- Children and those diagnosed in early adulthood who have diabetes not characteristic of type 1 or type 2 diabetes that occurs in successive generations (suggestive of an autosomal dominant pattern of inheritance) should have genetic testing for maturity-onset diabetes of the young (Category A)

Murphy, et al.

Murphy, et al (2023) performed a systematic review and issued an expert opinion on how to use precision diagnostics to identify individuals with monogenic diabetes. The article states that the following individuals should be offered testing for monogenic diabetes:

1. All patients diagnosed with diabetes before the age of 6 months should be tested for monogenic forms of neonatal diabetes using the large-gene panel.
2. All patients diagnosed between 6 and 12 months should be tested for monogenic forms of neonatal diabetes using the large-gene panel. No demonstrable yield of monogenic etiology to support reflexive genetic testing patients diagnosed with diabetes between 12-24 months.
3. Women with gestational diabetes and fasting glucose above 5.5 mmol/L without obesity* should be tested for GCK etiology.
4. Those with persisting, mild hyperglycemia (HbA1c 38–62 mmol/mol, or fasting glucose 5.5–7.8 mmol/L) at any age, in the absence of obesity* should be tested for GCK etiology.
5. People without obesity under the age of 30 years who are either autoantibody negative and/or have retained C-peptide levels should be tested for monogenic diabetes using a large-gene panel (p.10).

International Society for Pediatric and Adolescent Diabetes (ISPAD)

In 2022, the International Society for Pediatric and Adolescent Diabetes (ISPAD) released a clinical practice consensus guideline for the diagnosis and management of monogenic diabetes in children and adolescents. The statement includes the following recommendations for genetic testing in the setting of neonatal diabetes and maturity onset diabetes of the young:

“All infants diagnosed with diabetes in the first 6 months of life are recommended to have immediate molecular genetic testing. Genetic testing may be considered in infants diagnosed between 6 and 12 months, especially in those without islet autoantibodies or who have other features suggestive of a monogenic cause” (p. 1190).

"The diagnosis of maturity onset diabetes of the young (MODY) is recommended in the following scenarios: family history of diabetes in a parent and first-degree relatives of that affected parent in persons with diabetes who lack the characteristics of T1D and T2D" (p. 1191).

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Reviews, Revisions, and Approvals	Revision Date	Approval Date
Policy developed.	03/23	03/23
Semi-annual review. Updated title to reflect V1.2024 version. Overview, coding, reference-table, background and references updated. Throughout policy: replaced "coverage criteria" with "criteria. For MTHFR Variant Analysis: under I. added "but not limited to:". For Mitochondrial Genome Sequencing, Deletion/Duplication, and/or Nuclear Genes Panel: under I.B.1.i. removed "and deafness". For Other Covered Metabolic, Endocrine, and Mitochondrial Disorders Panel: under II. Added "and Molecular"; added II.3. "Autosomal dominant inheritance…". For Background and Rationale; Known Familial Variant Analysis for Metabolic, Endocrine, and Mitochondrial Disorders panel: replaced "inheritance patterns" with "genetic testing"; under MTHFR Variant Analysis: added ". Confirmed 2020".	10/23	10/23
Updated table, criteria section labels, and background for maturity-onset diabetes of the young to state "Monogenic diabetes of the young (including maturity-onset diabetes of the young (MODY))". Updated monogenic diabetes of the young criteria: In I.A., changed from requiring the diabetes diagnosis within the first six months of life to the first 12 months of life; in I.B., changed requirement for the member to have the diagnosis before age 35 years to age 30 years; reworded option for autoantibodies; reworded C-peptide criteria to remove specific values and the requirement for hypoglycemia; replaced criteria for specific features of atypical type 2 diabetes with "diagnosis of diabetes not characteristic of type 1 or type 2 diabetes"; removed requirement for inclusion of specific genes in the panel. Background for monogenic diabetes updated.	01/24	01/24
Semi-annual review. Updated title to reflect V2.2024 version. In Known Familial Variant Analysis for Metabolic, Endocrine, and Mitochondrial Disorders, moved criteria to policy "Genetic Testing: General Approach to Genetic and Molecular Testing" to consolidate criteria for known familial variant tests. In Monogenic Diabetes (Including Maturity-Onset Diabetes of the Young (MODY)) Panels, criteria set name changed (formerly "Maturity-Onset Diabetes of the Young	04/24	04/24

Reviews, Revisions, and Approvals	Revision Date	Approval Date
(MODY)"). Minor rewording for clarity throughout. Coding, reference-table, background and references updated.		
Semi-annual review. Updated title to reflect V1.2025. MTHFR Variant Analysis: Streamlined portions of Background and Rationale section for brevity.	11/24	11/24
New policy created; criteria previously in Concert Genetic Testing: Metabolic, Endocrine, and Mitochondrial Disorders. Semi-annual review with no change to criteria for Monogenic Diabetes (Including Maturity Onset Diabetes of the Young (MODY)) Panels except to change the "investigational" statement II to note that "current evidence does not support…". Coding table, rationale and references updated.	11/25	12/25

REFERENCES

1. Murphy R, Colclough K, Pollin TI, et al. The use of precision diagnostics for monogenic diabetes: a systematic review and expert opinion. *Commun Med (Lond)*. 2023;3(1):136. Published 2023 Oct 5. doi:10.1038/s43856-023-00369-8
2. Greeley SAW, Polak M, Njølstad PR, et al. ISPAD Clinical Practice Consensus Guidelines 2022: The diagnosis and management of monogenic diabetes in children and adolescents. *Pediatr Diabetes*. 2022;23(8):1188-1211. doi:10.1111/pedi.13426
3. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics. ACOG Practice Bulletin No. 201: Pregestational Diabetes Mellitus. Obstet Gynecol. 2018 Dec;132(6):e228-e248. doi: 10.1097/AOG.0000000000002960. PMID: 30461693
4. US Preventive Services Task Force. Screening for Prediabetes and Type 2 Diabetes: US Preventive Services Task Force Recommendation Statement. *JAMA.* 2021;326(8):736–743. doi:10.1001/jama.2021.12531
5. American Diabetes Association Professional Practice Committee. 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes-2024. Diabetes Care. 2024;47(Suppl 1):S20-S42. doi:10.2337/dc24-S002

6. American Diabetes Association Professional Practice Committee. 6. Glycemic Goals and Hypoglycemia: Standards of Care in Diabetes-2024. Diabetes Care. 2024;47(Suppl 1):S111-S125. doi:10.2337/dc24-S006

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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.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care and are solely responsible for the medical advice and treatment of member/enrollees. This clinical policy is not intended to recommend treatment for member/enrollees. Member/enrollees should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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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.