Policy Number	MED207.164
Policy Effective Date	04/01/2026

Laboratory Testing Investigational Services

Table of Contents
Coverage
Policy Guidelines
Description
Rationale
Coding
References
Policy History

Related Policies (if applicable)
None

Disclaimer

Carefully check state regulations and/or the member contract.
Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Coverage

All tests listed in this policy **are considered experimental, investigational and/or unproven** as there is insufficient evidence to determine that the technology results in an improvement in the net health outcome (see “Coding” section).

Policy Guidelines

Genetics Nomenclature Update
The Human Genome Variation Society nomenclature is used to report information on variants found in DNA and serves as an international standard in DNA diagnostics. It is being implemented for genetic testing medical evidence review updates starting in 2017 (see Table PG1). The Society’s nomenclature is recommended by the Human Variome Project, the Human Genome Organization, and by the Human Genome Variation Society itself.

The American College of Medical Genetics and Genomics and the Association for Molecular Pathology standards and guidelines for interpretation of sequence variants represent expert opinion from both organizations, in addition to the College of American Pathologists. These

recommendations primarily apply to genetic tests used in clinical laboratories, including genotyping, single genes, panels, exomes, and genomes. Table PG2 shows the recommended standard terminology to describe variants identified that cause Mendelian disorders.

Table PG1. Nomenclature to Report on Variants Found in DNA

Previous	Updated	Definition
Mutation	Disease-associated variant	Disease-associated change in the DNA sequence
	Variant	Change in the DNA sequence
	Familial variant	Disease-associated variant identified in a proband for use in subsequent targeted genetic testing in first-degree relatives

Table PG2. American College of Medical Genetics and Genomics and the Association for Molecular Pathology Standards and Guidelines for Variant Classification

Variant Classification	Definition
Pathogenic	Disease-causing change in the DNA sequence
Likely pathogenic	Likely disease-causing change in the DNA sequence
Variant of uncertain significance	Change in DNA sequence with uncertain effects on disease
Likely benign	Likely benign change in the DNA sequence
Benign	Benign change in the DNA sequence

Genetic Counseling

Experts recommend formal genetic counseling for patients who are at-risk for inherited disorders and who wish to undergo genetic testing. Interpreting the results of genetic tests and understanding risk factors can be difficult for some patients; genetic counseling helps individuals understand the impact of genetic testing, including the possible effects the test results could have on the individual or their family members. It should be noted that genetic counseling may alter the utilization of genetic testing substantially and may reduce inappropriate testing; further, genetic counseling should be performed by an individual with experience and expertise in genetic medicine and genetic testing methods.

Description

This policy applies if there is not a separate medical policy that outlines specific criteria for testing. If a separate medical policy does exist, then the criteria for medical necessity therein supersede the guidelines herein.

This policy addresses laboratory services considered to be experimental, investigational and/or unproven. These tests are often available on a clinical basis before the required and necessary evidence base to support clinical validity and utility is established. Because these tests are often proprietary, there may be no independent test evaluation data available in the early stages to support the laboratory's claims regarding test performance and utility. While studies using these tests may generate information that may help elucidate the biologic mechanisms of

disease and eventually help design treatments, the tests listed in this policy are currently in a developmental phase, with limited evidence of clinical utility for diagnosis, prognosis, or risk assessment.

Regulatory Status
Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.

Rationale

Medical policies assess whether a medical test is clinically useful. A useful test provides information to make a clinical management decision that improves the net health outcome. That is, the balance of benefits and harms is better when the test is used to manage the condition than when another test or no test is used to manage the condition.

The first step in assessing a medical test is to formulate the clinical context and purpose of the test. The test must be technically reliable, clinically valid, and clinically useful for that purpose. Medical policies assess the evidence on whether a test is clinically valid and clinically useful. Technical reliability is outside the scope of these policies, and credible information on technical reliability is available from other sources.

Laboratory Testing Investigational Services
Clinical Context and Test Purpose
The purpose of various commercially available genetic and molecular diagnostic, prognostic, and therapeutic tests for individuals with relevant indications is to inform a clinical management decision that improves the net health outcome.

No formal evidence review was conducted.

Practice Guidelines and Position Statements
National Human Genome Research Institute et al.
In 2021, the National Human Genome Research Institute's ClinGen Complex Disease Working Group updated the Genetic Risk Prediction (GRIPS) Reporting Statement in collaboration with the Polygenic Score (PGS) Catalog. (1) The 22-item reporting framework developed to define the minimal information needed to interpret and evaluate polygenic risk scores is summarized in Table 1.

Table 1. Polygenic Risk Score Reporting Statement

Reporting Standard

Background	Study Type
	Risk Model Purpose & Predicted Outcome
Study Population and Data	Study Design & Recruitment
	Participant Demographic and Clinical Characteristics
	Ancestry
	Genetic Data
	Non-Genetic Variables
	Outcomes of Interest
	Missing Data
Risk Model Development & Application	Polygenic Risk Score Construction & Estimation
	Risk Model Type
	Integrated Risk Model(s) Description & Fitting
Risk Model Evaluation	PRS Distribution
	Risk Model Predictive Ability
	Risk Model Discrimination
	Risk Model Calibration
	Subgroup Analyses
Limitations & Clinical Implications	Risk Model Interpretation
	Limitations
	Generalizability
	Risk Model Intended Uses
Data Transparency & Availability	

PRS: polygenic risk score.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	0616U, 0617U, 0618U, 0619U, 0620U, 0621U, 0622U, 0623U, 0624U, 0625U, 0626U, 0627U, 0629U, 0631U, 0634U, 0644U, 0645U, 0646U, 0647U, 0648U, 0650U, 0652U, 0653U, 0654U, 0655U, 0657U, 0658U, 0659U, 0663U, 0664U, 0666U, 0668U, 0669U, 0680U, 0681U, 0682U, 0683U, 0684U, 0685U, 0687U, 0692U, 0693U, 0694U, 0695U
HCPCS Codes	None

*Current Procedural Terminology (CPT®) ©2025 American Medical Association: Chicago, IL.

References

1. Wand H, Lambert SA, Tamburro C, et al. Improving reporting standards for polygenic scores in risk prediction studies. Nature. Mar 2021; 591(7849):211-219. PMID 33692554

Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision

Date	Description of Change
04/01/2026	New medical document. All tests listed in this policy are considered experimental, investigational and/or unproven as there is insufficient evidence to determine that the technology results in an improvement in the net health outcome (see “Coding” section).