Gene Expression Profiling for Noncancer Indications

INDEPENDENT CARE HEALTH PLAN

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Medicare Advantage Medical Coverage Policy

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Related Documents

Please refer to CMS website for the most current applicable CMS Online Manual System (IOMs)/National Coverage Determination (NCD)/ Local Coverage Determination (LCD)/Local Coverage Article (LCA)/ Transmittals.

Type	Title	ID Number	Jurisdiction Medicare Administrative Contractors (MACs)	Applicable States/Territories

LCD	MolDX: Envisia™, Veracyte™, Idiopathic Pulmonary Fibrosis Diagnostic Test	L37919	J5, J8 - Wisconsin Physicians Service Insurance Corporation	IA, IN, KS, MI, MO, NE
LCD	Molecular Pathology Procedures	L35000	J6, JK - National Government Services, Inc.	CT, IL, MA, ME, MN, NH, NY, RI, VT, WI
LCD	MolDX: Envisia™, Veracyte™, Idiopathic Pulmonary Fibrosis Diagnostic Test	L37905	J15 - CGS Administrators, LLC (Part A/B MAC)	KY, OH
LCD	MolDX: Envisia™, Veracyte™, Idiopathic Pulmonary Fibrosis Diagnostic Test	L37887	JE - Noridian Healthcare Solutions, LLC	CA, HI, NV, American Samoa, Guam, Northern Mariana Islands
LCD	MolDX: Envisia™, Veracyte™, Idiopathic Pulmonary Fibrosis Diagnostic Test	L37891	JF - Noridian Healthcare Solutions, LLC	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY
LCD	MolDX: Envisia™, Veracyte™, Idiopathic Pulmonary Fibrosis Diagnostic Test	L37857	JJ, JM - Palmetto GBA	AL, GA, NC, SC, TN, VA, WV
LCD	Molecular Pathology Procedures	L34519	JN - First Coast Service Options, Inc.	FL, PR, U.S. VI

Description

Gene expression profiling (GEP) is a laboratory test that measures the activity, or expression, of ribonucleic acid (RNA) of hundreds to thousands of genes at one time to give an overall picture of gene activity. GEP tests are typically performed on tumor tissue but may also be performed on other specimens such as blood. These tests often use microarray technology though other methodologies, such as next generation sequencing (NGS), whole transcriptome sequencing and reverse transcription polymerase chain reaction (RT-PCR), are also used. GEP tests are currently offered primarily for the management of cancer, most notably breast. However, the scope of testing has broadened to include evaluation of idiopathic pulmonary fibrosis. An example of this type of testing is **Envisia Genomic Classifier**.

GEP tests differ from germline genetic tests. GEP tests analyze RNA which is dynamic, responds to cellular environmental signals, are not usually representative of an individual's germline DNA and are not inheritable. Germline genetic testing analyzes an individual's deoxyribonucleic acid (DNA) to detect genetic variants (mutations). Germline mutations are inherited, are constant throughout an individual's lifetime and are identical in every cell of the body.

Coverage Determination

iCare follows the CMS requirements that only allows coverage and payment for services that are reasonable and necessary for the diagnosis and treatment of illness or injury or to improve the functioning of a malformed body member except as specifically allowed by Medicare.

Genetic tests must demonstrate clinical utility, analytical and clinical validity and fulfill the CMS "reasonable and necessary" criteria. Analytic validity (test accurately identifies the gene variant), clinical validity (test identifies or predicts the clinically defined disorder) and clinical utility (test measurably improves clinical outcomes) of the genetic test is supported by generally accepted standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, specialty society recommendations, and views of physicians practicing in relevant clinical areas. The test must be ordered by a physician who is treating the beneficiary and the results will be used in the management of a beneficiary's specific medical problem.

For jurisdictions with no Medicare guidance for a particular test, iCare will utilize the MolDX program and Technical Assessments for molecular assays as the standard to evaluate clinical utility, analytical and clinical validity in conjunction with adhering to Medicare's reasonable and necessary requirement.

In interpreting or supplementing the criteria above and in order to determine medical necessity consistently, iCare may consider the following criteria:

Envisia Genomic Classifier (81554) will be considered medically reasonable and necessary when the following requirements are met:[1,2,3,4,5]

- Individual to be tested has interstitial lung disease (ILD) and is suspected of having idiopathic pulmonary fibrosis (IPF); **AND**
- Absence of a definitive occupational, environmental, medication-related or other cause of the individual's lung disease; **AND**
- Exclusion of autoimmune disease by clinical evaluation and serologic testing, including an evaluation by a rheumatologist when indicated; **AND**
- High-resolution computed tomography (CT) scan of the chest (defined by high kernel approximately 1mm axial reconstructions, including both inspiratory and expiratory imaging) and shows one of the following:
    - A probable interstitial pneumonia (UIP) pattern as defined by the Diagnostic Categories of UIP Based on CT Patterns; **OR**
    - An indeterminate UIP pattern Diagnostic Categories of UIP Based on CT Patterns; **AND**
- Is healthy enough to undergo a bronchoscopy with transbronchial biopsies

The use of the criteria in this Medicare Advantage Medical Coverage Policy provides clinical benefits highly likely to outweigh any clinical harms. Services that do not meet the criteria above are not medically

necessary and thus do not provide a clinical benefit. Medically unnecessary services carry risks of adverse outcomes and may interfere with the pursuit of other treatments which have demonstrated efficacy.

Coverage Limitations

US Government Publishing Office. Electronic code of federal regulations: part 411 – 42 CFR § 411.15 - Particular services excluded from coverage

The following tests may not be considered a benefit (statutory exclusion):

- Tests considered screening in the absence of clinical signs and symptoms of disease that are not specifically identified by the law;[11] **OR**
- Tests that confirm a diagnosis or known information;[11] **OR**
- Tests to determine risk for developing a disease or condition;[11] **OR**
- Tests performed to measure the quality of a process;[11] **OR**
- Tests without diagnosis specific indications;[11] **OR**
- Tests identified as investigational by available literature and/or the literature supplied by the developer and are not a part of a clinical trial[11]

These treatments and services fall within the Medicare program's statutory exclusion that prohibits payment for items and services that have not been demonstrated to be reasonable and necessary for the diagnosis and treatment of illness or injury (§1862(a)(1) of the Act). Other services/items fall within the Medicare program's statutory exclusion at 1862(a)(12), which prohibits payment.

The following items will not be considered medically reasonable and necessary:

- Genetic tests that have not demonstrated clinical utility, analytical and clinical validity via the MolDX Program

A review of the current medical literature shows that the evidence is insufficient to determine that these services are standard medical treatments. There remains an absence of randomized, blinded clinical studies examining benefit and long-term clinical outcomes establishing the value of these services in clinical management.

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
81493	Coronary artery disease, mRNA, gene expression profiling by real-time RT-PCR of 23 genes, utilizing whole peripheral blood, algorithm reported as a risk score	
81554	Pulmonary disease (idiopathic pulmonary fibrosis [IPF]), mRNA, gene expression analysis of 190 genes, utilizing transbronchial biopsies, diagnostic algorithm reported as categorical result (eg, positive or negative for high probability of usual interstitial pneumonia [UIP])	
0318U	Pediatrics (congenital epigenetic disorders), whole genome methylation analysis by microarray for 50 or more genes, blood	
CPT® Category III Code(s)	**Description**	**Comments**
No code(s) identified		
HCPCS Code(s)	**Description**	**Comments**
No code(s) identified		

References

1. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: Envisia™, Veracyte™, Idiopathic Pulmonary Fibrosis Diagnostic Test (L37857). https://www.cms.gov. Published April 1, 2019. Updated June 29, 2023. Accessed September 19, 2023.

2. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: Envisia™, Veracyte™, Idiopathic Pulmonary Fibrosis Diagnostic Test (L37887). https://www.cms.gov. Published May 27, 2019. Updated June 29, 2023. Accessed September 19, 2023.

3. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: Envisia™, Veracyte™, Idiopathic Pulmonary Fibrosis Diagnostic Test (L37891). https://www.cms.gov. Published May 27, 2019. Updated June 29, 2023. Accessed September 19, 2023.

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6. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). Molecular pathology procedures (L34519). https://www.cms.gov. Published October 1, 2015. Updated December 12, 2021. Accessed October 2, 2023.

7. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). Molecular pathology procedures (L35000). https://www.cms.gov. Published October 1, 2015. Updated August 6, 2023. Accessed October 2, 2023.

8. ECRI Institute. ECRI Genetic Test Assessment. Envisia Genomic Classifier (Veracyte, Inc.) for diagnosing idiopathic pulmonary fibrosis. https://www.ecri.org. Published June 2021. Accessed March 7, 2023.

9. Hayes, Inc. Molecular Test Assessment. Envisia Genomic Classifier (Veracyte). https://evidence.hayesinc.com. Published March 5, 2020. Updated March 3, 2023. Accessed April 17, 2023.

10. Lynch DA, Sverzellati N, Travis WD, et al. Diagnostic criteria for idiopathic pulmonary fibrosis: a Fleischner Society white paper. *Lancet Respir Med*. 2018;6(2):138-153. https://www.thelancet.com. Accessed September 18, 2023.

11. Palmetto GBA. Molecular diagnostic program (MolDX®): coverage, coding, and pricing standards and requirements (M00106). https://www.palmettogba.com/MolDx. Published December 2019. Accessed September 27, 2023.

Appendix

Appendix A

Diagnostic Categories of UIP Based on CT Patterns[10]

Distribution and Features	Typical UIP CT Pattern	Probable UIP CT Pattern	CT Pattern Indeterminate for UIP	CT Features Most Consistent With Non-IPF Diagnosis
Distribution	Basal predominant (occasionally diffuse), and subpleural predominant; distribution is often heterogeneous	Basal and subpleural predominant; distribution is often heterogeneous	Variable or diffuse	Upper-lung or mid-lung predominant fibrosis; peribronchovascular predominance with subpleural sparing
Features	Honeycombing; reticular pattern with peripheral traction bronchiectasis or bronchiolectasis*****; absence of features to suggest an alternative diagnosis	Reticular pattern with peripheral traction bronchiectasis or bronchiolectasis*****; honeycombing is absent; absence of features to suggest an alternative diagnosis	Evidence of fibrosis with some inconspicuous features suggestive of non-UIP pattern	Any of the following: predominant consolidation, extensive pure ground glass opacity (without acute exacerbation), extensive mosaic attenuation with extensive sharply defined lobular air trapping on expiration, diffuse nodules or cysts

*****Reticular pattern is superimposed on ground glass opacity, and in these cases it is usually fibrotic. Pure ground glass opacity, however, would be against the diagnosis of UIP or IPF and would suggest acute exacerbation, hypersensitivity pneumonitis, or other conditions

Change Summary

- 01/01/2024 New Policy.