Gene Expression Profiling

Medical Guideline Disclaimer

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Definitions

Gene expression profiling (GEP) is a technology for identifying the genes that are active in a given sample of cells or tissue. This technique enables profiling of genes that are differentially expressed in disease states; thereby providing diagnostic and prognostic information.

Note: This guideline includes gene expression analysis, gene sequencing, and other techniques.

Related Medical Guidelines

• AlloMap® Molecular Expression Testing for Post-Heart-Transplant Rejection
• Analysis of KRAS Status
• Epidermal Growth Factor Receptor Mutation Analysis for Patients with Non-Small-Cell Lung Cancer
• BCR-ABL1 Genetic Mutation Testing in Chronic Myelogenous Leukemia and Acute Lymphoblastic Leukemia
• BRAF Mutation Analysis
• BRCA 1 and 2 Genetic Testing (Sequence Analysis/Rearrangement)
• Cardiac Ion Channel Genetic Testing
• Carrier Screening for Parents or Prospective Parents
• Chromosomal Microarray Analysis (CMA)
• Gene Expression Profiling and Biomarker Testing for Breast Cancer
• Gene Expression Profiling of Melanomas
• Gene Expression Testing for Multiple Myeloma
• Genetic Analysis of PIK3CA Status in Tumor Cells
• Genetic Counseling and Testing
• Genetic Testing for Alzheimer’s disease
• Genetic Testing for Cancer Susceptibility
• Genetic Testing for Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL) Syndrome
• Genetic Testing for Colorectal Cancer/Lynch Syndrome
• Genetic Testing for Cystic Fibrosis
• Genetic Testing for Factor V Leiden Mutation Analysis
• Genetic Testing for Frontotemporal Dementia (FTD)
• Genetic Testing for Hereditary Cardiomyopathy
• Genetic Testing for Hereditary Hemochromatosis
Genetic Testing for Hereditary Pancreatitis
Genetic Testing for Inherited Peripheral Neuropathies
Genetic Testing for PTEN Hamartoma Tumor Syndrome
Genetic Testing for RET Proto-Oncogene Germline Mutations
Genetic Testing for Statin-Induced Myopathy
Genetic Testing for TP53 Mutations (Li-Fraumeni Syndrome)
Janus Kinase 2 (JAK2) V617F Gene Mutation Assay

Guideline

Members are eligible for GEP testing as follows:

I. Advanced cancer; next generation sequencing (NGS), when performed with a diagnostic lab test that has received FDA approval or clearance (e.g., Foundation One CDx)
   Covered for Medicare members only when the following criteria are met:
   1. Member has
      i. either recurrent, relapsed, refractory, metastatic, or advanced stages III or IV cancer; and
      ii. either not been previously tested using the same NGS test for the same primary diagnosis of cancer or repeat testing using the same NGS test only when a new primary cancer diagnosis is made by the treating physician; and
      iii. decided to seek further cancer treatment (e.g., therapeutic chemotherapy).
   2. The diagnostic laboratory test using NGS must have:
      i. FDA approval or clearance as a companion in vitro diagnostic; and
      ii. an FDA approved or cleared indication for use in that patient’s cancer; and
      iii. results provided to the treating physician for management of the patient using a report template to specify treatment options.

II. Breast cancer; one of the following
(See EmblemHealth Gene Expression Profiling and Biomarker Testing for Breast Cancer Medical Guideline)
   1. Breast Cancer Index®
   2. EndoPredict®
   3. HerMark® (Covered for Medicare members only)
   4. MammaPrint®
   5. Oncotype DX®
   6. Prosigna® Breast Cancer Prognostic Gene Signature Assay

III. Post-heart-transplant rejection; allowable every 1–3 months
(See EmblemHealth AlloMap Medical Guideline)

IV. Thyroid lesions with indeterminate cytology; one-time testing
   1. Afirma Thyroid FNA Analysis®
   2. ThyGenX (formerly miRInform®)
   3. ThyraMIR Thyroid miRNA classifier
   4. ThyroSeq next generation sequencing

V. Uveal melanoma (DecisionDx covered for Medicare members only)
(See EmblemHealth Gene Expression Profiling of Melanomas Medical Guideline)
Limitations/Exclusions

I. Gene expression profiling is not considered medically necessary in the absence of the following:
   1. Analytical/clinical validity
   2. Clinical utility (i.e., result does not impact medical management; e.g., surgery, change in surveillance, chemotherapy, hormonal manipulation, etc.)

II. Confirmation of consumer-based testing (including, but not limited to Health + Ancestry [23andMe] has not been shown to be of clinical value and remains experimental/investigational. Testing will be approved only for members who otherwise meet the clinical criteria in these policies

III. Whole exome sequencing and whole genome sequencing are not considered medically necessary due to insufficient evidence of therapeutic value for all indications, including but not limited to:
   1. Diagnosis in members with suspected genetic disorders
   2. Population-based screening
   3. Cancer testing to identify targeted therapies
   4. Preimplantation genetic diagnosis and screening
   5. Invasive prenatal (fetal) testing
   6. Products of conception and pregnancy loss
   7. Testing for chromosomal rearrangements

IV. The following GEP tests are not considered medically necessary due to insufficient evidence of therapeutic value (list not all-inclusive):
   1. 23-Gene NGS Pyruvate Metabolism and Related Disorders Panel
   2. 23andMe Health + Ancestry Service
   3. ADmark® Alzheimer’s Evaluation
   4. Albinism Panel
   5. AmHPR Helicobacter Pylori Antibiotic Resistance NGS Panel
   6. Autosomal Dominant and Recessive Polycystic Kidney Disease Nextgen Sequencing (NGS) Panel
   7. Avise tests
      i. Avise® CTD
      ii. Avise® MTX (aka Avise PG) (Covered for Medicare members only)
      iii. Avise® Lupus
   8. bioTheranostics Cancer TYPE ID (Covered for Medicare members only)
   9. BRCAPlus
   10. BluePrint®
   11. BreastNext™
   12. BreastOncPx™
   13. BreastPRS
   14. BREVAGen/BREVAGenplus
   15. CancerNext, CancerNext-Expanded™
   16. CancerTYPE ID® (Covered for Medicare members only)
   17. Carbohydrate Metabolism Deficiency NextGen DNA Screening Panel
   18. Cardiovascular Health Panel
   19. CGD Universal Test Panel
   20. Ciliopathies: Sequencing Panel
21. Ciliopathy NextGen Sequencing (NGS) Panel
22. ColoNext™
23. ColoVantage
24. Combined Cardiac Panel (Covered for Medicare members only)
25. Complete Hereditary Spastic Paraplegia Evaluation Panel
26. Complete Lung
27. Comprehensive Dystonia NextGen DNA Screening Panel
28. Comprehensive Inherited Retinal Dystrophies Sequencing Panel
29. Comprehensive Molecular Genetic Panel
   Comprehensive Muscular Dystrophy/Myopathy Next Generation DNA Sequencing Panel
30. Comprehensive Molecular Genetic Panel
31. ConfirmMDx™ (Covered for Medicare members only)
32. Congenital Myopathy NextGen Sequencing (NGS) Panel
33. Congenital Stationary Night Blindness panel
34. Connective Tissue NGS Panel
35. Corus® CAD (Covered for Medicare members only)
36. Counsyl Foresight Carrier Screen
37. Craniosynostosis next generation sequencing (NGS) panel
38. DecisionDx tests
   i. Glioblastoma
   ii. Uveal melanoma (Covered for Medicare members only)
39. Decipher® Prostate Classifier (Covered for Medicare members only)
40. DecodEX Microbial Genetic Identification
41. Distal Hereditary Motor Neuropathy NextGen Sequencing (NGS) Panel
42. Ehlers-Danlos Syndrome NGS Panel Dominant and Recessive
43. ENGAUGE™-cancer-DLBCL
44. Epi proColon
45. ExomeNext
46. ExomeNext-Rapid
47. Expanded Pan-Ethnic Panel
48. Familial Hemiplegic Migraine NextGen Sequencing (NGS) Panel Fetal Akinesia
   Deformation Sequence/Lethal Multiple Pterygium Syndrome NextGen Sequencing (NGS)
   Panel
49. FoundationOne CDx (Covered for Medicare members only)
50. GeneAware
51. GeneFx® Colon
52. GeneFx® Lung
53. GeneKey
54. GeneStrat™
55. GeneSight (Covered for Medicare members only)
56. GeneTrails® Solid Tumor Panel
57. GPS Cancer
58. Guardant 360® Panel
59. Healthy Weight DNA Insight
60. Healthy Woman DNA Insight
61. HCMNext
62. H/I Gene Expression Ratio
63. Hemophagocytic Lymphohistiocytosis Panel by next generation sequencing (NGS)
64. Hereditary Spherocytosis/Elliptocytosis NextGen Sequencing Panel
65. HERmark (Covered for Medicare members only)
66. HLA-DQB1*06:02 typing for the diagnosis or management of narcolepsy
67. HOX13:IL17BR
68. Hypokalemic and Hyperkalemic Periodic Paralysis Disorders NGS Sequencing Panel
69. Insight® DX Breast Cancer Profile
70. Intellectual Disability (IDNEXT) Panel
71. Leukoencephalopathy NGS Panel
72. Lipodystrophy NGS Panel
73. LUNGSEQ® Panel
74. Macula Risk PGx
75. Macular Degeneration Mutation Analysis
76. Mammastatin
77. miReview®
78. Mammastrat
79. Melaris®
80. Molecular Intelligence
81. My5-FU™ (previously OnDose™)
82. Myeloid Molecular Profile
83. myPath®
84. MyPRS® Myeloma Prognostic Risk Signature
85. myRisk™
86. MYvantage® Hereditary Comprehensive Cancer Panel
87. Neurotransmitter Metabolism Deficiency NextGen DNA Screening Panel
88. Next Gen RASopathy Panel
89. Next Generation Sequencing Panel for ASXL1, RECQL4, RNU4ATAC, SOX2
90. NextStepDx PLUS®
91. NGS Epilepsy/Seizure Panel
92. NGS RASopathy Panel
93. OmniSeq Comprehensive
94. Oncotype DX® tests
   i. Breast DCIS
   ii. Colon cancer (Covered for Medicare members only)
   iii. Prostate cancer (Covered for Medicare members only)
95. Oncofocus®
96. OnkoMatch™
97. OncoVantage™
98. Oncovue
99. OPA 1 gene sequencing for autosomal dominant optic atrophy and/or optic neuropathy
100. Osteogenesis Imperfecta NGS Panel-Recessive
101. OvaNext™
102. Overa (aka OVA1 Next Generation or second-generation Multivariate Index Assay [MIA2G] test)
103. PAM50 Breast Cancer Intrinsic Classifier™
104. PancNext™
105. PancraGEN (previously Pathfinder TG®) (Medicare only)
106. Panexia®
107. Paradigm Cancer Diagnostics [PCDx] Test
108. Pediatric Neurology Region of Interest Trio
109. Percepta Bronchial Genomic Classifier (Covered for Medicare members only)
110. Pervenio™ Lung NGS
111. Pontocerebellar Hypoplasia Panel
112. Post-Op Px™ (formerly the Prostate Px Plus)
113. Preparent Global Panel
114. Previstage™
115. Progenity CFnxt
116. Progenity® Pan-Ethnic Carrier Screening Panel
117. PROGENSA® PCA3 (Covered for Medicare members only)
118. Prolaris® (Covered for Medicare members only)
119. ProMark Risk Score for prostate cancer (Covered for Medicare members only)
120. ProOnc TumorSource DX
121. Proove profile panels (e.g., Opioid Risk Panel)
122. ProstateNext
123. RenalNext™
124. ResponseDX Tissue Origin Test Rotterdam/Veridex (Medicare only)
125. RetnaGene AMD
126. Rotterdam Signature
127. Saethre-Chotzen Syndrome (TWIST) Sequencing and MLPA (Greenwood Genetic Center)
128. ScolioScore™ AIS Prognostic Test
129. SelectMDx for prostate cancer
130. Spastic Paraplegia Next Generation Sequencing Panel
131. Stickler Syndrome NGS Panel
132. SymGene68™ Next Generation Sequencing Cancer Panel
133. SYMPHONY™ Genomic Breast Cancer Profile (combines BluePrint, MammaPrint and TargetPrint tests)
134. Skeletal Dysplasia Ciliopathy NGS Panel
135. SYMPHONY™ Personalized Breast Cancer Genomic Profile
136. TAAADNext
137. Target Now™ molecular profiling test (aka MI Profile, MI Profile X)
138. TargetPrint®
139. TheraPrint®
140. theraseek Sequence Analysis for Functional Disorders
141. Thrombocytopenia NextGen Sequencing (NGS) Panel
142. TruGenome Undiagnosed Disease Test
143. TruGenome Technical Sequence Data (whole exome sequencing test for labs and physicians who will make their own clinical interpretations make their own clinical interpretations)
144. Universal Carrier Panel
145. Vectra DA (Covered for Medicare members only)
146. Vitreoretinopathy NGS Panel

Revision History

<table>
<thead>
<tr>
<th>Date</th>
<th>Description</th>
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<tbody>
<tr>
<td>4/13/2018</td>
<td>Added FoundationOne CDx test coverage for Medicare members</td>
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<tr>
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<td>Removed the following test, Thyroid, FNA Cytomorphology with Molecular tests (Quest), from the list of covered tests for thyroid lesions with indeterminate cytology (no longer available from Quest)</td>
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<td>Added language communicating noncoverage of testing to confirm results of consumer-based testing</td>
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<tr>
<td></td>
<td>Added language clarifying that whole exome and whole genome sequencing is considered investigational</td>
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<tr>
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<td>Updated list of lab tests regarded as investigational</td>
</tr>
<tr>
<td>4/14/2017</td>
<td>Added ThyraMIR Thyroid miRNA classifier to list of eligible tests for thyroid lesions with indeterminate cytology</td>
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<tr>
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<td>Added Melarisi to investigational list</td>
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<tr>
<td>2/10/2017</td>
<td>Added the following tests to investigational list: Oncofocus®, Previstage™</td>
</tr>
<tr>
<td>9/9/2016</td>
<td>Added the following tests to investigational list: DecodEX, Oncovue, OvaNext™, Panexia®</td>
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<td>Date</td>
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<tr>
<td>8/12/2016</td>
<td>Added Medicare coverage for CancerTYPE ID.</td>
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<td>Added the following tests to investigational list: BrevaGEN/BrevaGEN plus, My5-FU™ (previously OnDose™), OncoVantage™, OPA 1 gene sequencing for autosomal dominant optic atrophy and/or optic neuropathy, Proove Opioid Risk Test</td>
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<tr>
<td>7/8/2016</td>
<td>Added the following tests to investigational list: Combined Cardiac Panel, Counsyl preconception carrier genetic screening, miReview®, Myeloid Molecular Profile, Paradigm Cancer Diagnostics [PCDx] Test, Pediatric Neurology Region of Interest Trio, Progenity® Pan-Ethnic Carrier Screening Panel, Rotterdam Signature, Saethre-Chotzen Syndrome (TWIST) Sequencing and MLPA, SelectMDx for prostate cancer</td>
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<tr>
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<td>Added GeneStrat and Molecular Intelligence to list of investigational tests.</td>
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<td>Reinstate coverage of the following tests for Medicare members:  Corus® CAD, ConfirmMDx™, Decipher® Prostate Classifier, Oncotype DX® Colon, Oncotype DX® prostate, Prolaris® and ResponseDX Tissue Origin Test</td>
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<tr>
<td>4/8/2016</td>
<td>Tests no longer covered for Medicare members (NGS Medicare Molecular Pathology LCD effective 4/1/2016) — Corus® CAD, ConfirmMDx™, Decipher® Prostate Classifier, Oncotype DX® Colon, Oncotype DX® prostate, Prolaris® and ResponseDX Tissue Origin Test.</td>
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<td>Non-covered tests added to investigational list — GeneFx® Colon, myPath® (NGS Medicare Molecular Pathology LCD effective 4/1/2016)</td>
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<tr>
<td>12/21/2015</td>
<td>Amended Limitations/Exclusions Section to reflect positive Medicare coverage for Oncotype Prostate.</td>
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<tr>
<td>10/9/2015</td>
<td>Amended Limitations/Exclusions Section to reflect positive Medicare coverage for Decipher Prostate Classifier and Prolaris</td>
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**References**


Specialty-matched clinical peer review.