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Originated Department	Medical Management

Next Generation Sequencing (NGS) Genetic Testing

Audience
Medical Management, Claims

Purpose

Medical policies provide general support for applying Mountain Health Co-Op member policy document coverage decisions, and the member-specific benefit plan document must be referenced. The terms of the member-specific Policy document may differ from the standard benefit plan based on this medical policy. If there is a conflict between a member-specific policy document and the Mountain Health Co-Op medical policy, the document supersedes this policy. Any person(s) applying this medical policy must identify member eligibility, the member-specific policy document, and related policies or guidelines before applying this medical policy, including the existence of any state or federal guidance. Mountain Health Co-Op medical policies are designed for informational purposes only and are not an authorization, explanation of benefits, or contract. Receipt of benefits is subject to the satisfaction of all terms and conditions of the member-specific policy document coverage. Mountain Health Co-Op reserves the sole discretionary right to modify all policies and guidelines at any time.

Definition

Next-generation sequencing (NGS), also called second-generation sequencing, massively parallel sequencing, or massively parallel sequencing, is one of several high-throughput approaches to DNA sequencing that use the concept of massively parallel processing. These technologies use miniaturized and parallelized platforms to sequence 1 million to 43 billion short reads (50- 400 bases each) per instrument run.

Many NGS platforms differ in engineering configurations and sequencing chemistry. They share the technical paradigm of massively parallel sequencing via spatially separated, clonally amplified DNA templates or single DNA molecules in a flow cell. This design is very different from that of Sanger sequencing—also known as capillary sequencing or first-generation

sequencing—based on electrophoretic separation of chain-termination products produced in individual sequencing reactions.

NGS can be used to analyze DNA and RNA samples and is a popular tool in functional genomics. In contrast to microarray methods, NGS-based approaches have several advantages, including:

1. A priori knowledge of the genome or genomic features is not required;
2. Single-nucleotide resolution;
3. The possibility to detect related genes (or features), alternatively spliced transcripts, allelic gene variants and single nucleotide polymorphisms;
4. Higher dynamic range of signal;
5. Requires less DNA/RNA as input (nanograms of materials are sufficient); and
6. Higher reproducibility

NGS testing is commonly employed for cancer indications but is also used as a technique to assess other non-cancerous somatic (spontaneous) and germline (inheritable) conditions. Next- generation sequencing (NGS) allows for querying the entire genome (whole genome), the exons within all known genes (whole exome), or only exons of selected genes (target panel)

Targeted (aka Hot Spot) Tumor Panels

"Targeted NGS panels identify somatic alterations known to occur in certain areas (i.e., 'hotspots') in specific genes of interest. Generally, these NGS panels can detect single nucleotide variants (SNVs or point mutations) and small (typically ≤40 bp) insertions or deletions (indels), but not copy number alterations (CNAs) or structural variants (SVs), such as gene rearrangements, fusions, or translocations. These alterations typically represent genomic targets with corresponding targeted cancer therapies. Identifying a somatic alteration guides use of the corresponding targeted therapy." -Centers for Medicare and Medicaid Services (CMS) in 2018.

Comprehensive Genomic Profile (CGP) Testing

CGP is often described as NGS-based testing using complex and usually proprietary bioinformatics in a single test optimized to identify all molecular alterations (i.e., SNVs, small and large indels, CNAs, and SVs) in cancer-related genes. Microsatellite instability and tumor mutational burden may also be included in CGP testing.

Policy/Procedure

Mountain Health Co-Op reimburses Next Generation Sequencing (NGS) testing in specific circumstances as outlined.

A. Targeted Tumor Panels

i. Test was approved through the plan prior authorization process

ii. The test was billed using one of the following CPT codes most consistent with the number of genes tested:

a. 81445, Targeted genomic sequence analysis panel, solid organ neoplasm, DNA analysis, and RNA analysis when performed, 5-50 genes (eg, ALK, BRAF,

CDKN2A, EGFR, ERBB2, KIT, KRAS, NRAS, MET, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed

b. 81450, Targeted genomic sequence analysis panel, hematolymphoid neoplasm or disorder, DNA analysis, and RNA analysis when performed, 5-50 genes (eg, BRAF, CEBPA, DNMT3A, EZH2, FLT3, IDH1, IDH2, JAK2, KRAS, KIT, MLL, NRAS, NPM1, NOTCH1), interrogation for sequence variants, and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed
c. 81455, Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm, DNA analysis, and RNA analysis when performed, 51 or greater genes (eg, ALK, BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MLL, NPM1, NRAS, MET, NOTCH1, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed

iii. The test is performed to assess either solid organ or hematolymphoid neoplasms
iv. No more specific or proprietary CPT (XXXXU) code exists that reflects the testing performed

Mountain Health Co-Op reimburses for NGS panels

The units of service (UOS) for an NGS panel is one (UOS=1).

Laboratories with 1 to 4 gene(s) on their targeted NGS panel should use CPT® 81479 and one (1) UOS along with their test identifier (DEX Z-Code TM) to represent this service on their claims.

Tier 1 and/or Tier 2 individual biomarker CPT codes should not be used for a single gene or any combination of genes when testing is performed as part of a NGS or other multiplexing technology panel.

Mountain Health Co-Op may reimburse for Comprehensive Genomic Profile (CGP) testing if CPT code 81479 is used to report this service if testing is not considered investigational and medical necessity standards are met.

Mountain Health Co-Op will NOT reimburse for Comprehensive Genomic Profile (CGP) testing if CPT codes 81445, 81450, and/or 81455 are used to report this service. Use of codes 81445, 81450, and/or 81455 is inappropriate to use because the description of those codes does not include identification of specific molecular alterations (i.e., SNVs, small (≤40 bp) and large (> 40 bp) indels, CNAs, and SVs) which are included in CGP testing.

Applicable Coding

CPT Codes

Possibly Covered

81445	Targeted genomic sequence analysis panel, solid organ neoplasm, DNA analysis, and RNA analysis when performed, 5-50 genes (eg, ALK, BRAF, CDKN2A, EGFR, ERBB2, KIT, KRAS, NRAS, MET, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed
81450	Targeted genomic sequence analysis panel, hematolymphoid neoplasm or disorder, DNA analysis, and RNA analysis when performed, 5-50 genes (eg, BRAF, CEBPA, DNMT3A, EZH2, FLT3, IDH1, IDH2, JAK2, KRAS, KIT, MLL, NRAS, NPM1, NOTCH1), interrogation for sequence variants, and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed
81455	Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm, DNA analysis, and RNA analysis when performed,81445 or greater genes (eg, ALK, BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MLL, NPM1, NRAS, MET, NOTCH1, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed
81479	Unlisted molecular pathology procedure

Not Covered

0456U	Autoimmune (rheumatoid arthritis), next-generation sequencing (NGS), gene expression testing of 19 genes, whole blood, with analysis of anti-cyclic citrullinated peptides (CCP) levels, combined with sex, patient global assessment, and body mass index (BMI), algorithm reported as a score that predicts nonresponse to tumor necrosis factor inhibitor (TNFi) therapy
0467U	Oncology (bladder), DNA, next-generation sequencing (NGS) of 60 genes and whole genome aneuploidy, urine, algorithms reported as minimal residual disease (MRD) status positive or negative and quantitative disease burden
0473U	Oncology (solid tumor), next-generation sequencing (NGS) of DNA from formalin-fixed paraffin-embedded (FFPE) tissue with comparative sequence analysis from a matched normal specimen (blood or saliva), 648 genes, interrogation for sequence variants, insertion and deletion alterations, copy number variants, rearrangements, microsatellite instability, and tumor-mutation burden
0474U	Hereditary pan-cancer (eg, hereditary sarcomas, hereditary endocrine tumors, hereditary neuroendocrine tumors, hereditary cutaneous melanoma), genomic sequence analysis panel of 88 genes with 20 duplications/deletions using next-generation sequencing (NGS), Sanger

	sequencing, blood or saliva, reported as positive or negative for germline variants, each gene
0475U	Hereditary prostate cancer-related disorders, genomic sequence analysis panel using next-generation sequencing (NGS), Sanger sequencing, multiplex ligationdependent probe amplification (MLPA), and array comparative genomic hybridization (CGH), evaluation of 23 genes and duplications/deletions when indicated, pathologic mutations reported with a genetic risk score for prostate cancer

HCPCS Codes

No applicable codes

References

1. (Centers for Medicare and Medicaid Services, 2024). CMS.gov.https://www.cms.gov/medicare-coverage-database/details/article-details.aspx?articleId=55624&ver=17&LCDId=38119&DocID=L38119&bc=gAAAAAgAIAAAA AAA&
2. (National Cancer Institute) https://www.cancer.gov/publications/dictionaries/genetics-dictionary/def/next-generation-sequencing
3. American Medical Association, CPT Professional Edition (2024)

Vendors

- Health Plan Services (HPS)

Review/Revision/Approval History

Date	Description
07/01/2024	**New Policy**

Disclaimer

This document is for informational purposes only and should not be relied on in the diagnosis and care of individual patients. Medical and Coding/Reimbursement policies do not constitute medical advice, plan preauthorization, certification, an explanation of benefits, or a contract. Members should consult appropriate healthcare providers for medical advice, care, and treatment. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the member's benefit plan, effective when services are rendered.

The codes for treatments and procedures applicable to this policy are included for informational purposes. Including or excluding a procedure, diagnosis, or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as they apply to an individual member.