Next Generation Sequencing (NGS) Genetic Testing

Policy REIMB-007

Origination Date: 07/28/2021

Reviewed/Revised Date: 08/23/2023

Next Review Date: 08/23/2024

Current Effective Date: 08/23/2023

Disclaimer:

1. Policies are subject to change in accordance with State and Federal notice requirements.
2. Policies outline coverage determinations for U of U Health Plans Commercial and Healthy U (Medicaid) plans. Refer to the "Policy" section for more information.
3. Services requiring prior-authorization may not be covered, if prior-authorization is not obtained.
4. This Medical Policy does not guarantee coverage or payment of the service. The service must be a benefit in the member's plan and the member must be eligible for coverage at the time of service. Additional payment guidelines may be applied that are not included in this policy.

Description:

Next-generation sequencing (NGS), also called second-generation sequencing, massive parallel sequencing or massively parallel sequencing is any of several high-throughput approaches to DNA sequencing using the concept of massively parallel processing. These technologies use miniaturized and parallelized platforms for sequencing of 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 massive 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—that is 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 employed as a technique to assess for other non-cancerous somatic (spontaneous) and germ-line (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. Identification of 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 often proprietary bioinformatics in a single test that has been optimized to identify all types of 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 Statement and Criteria

1. Commercial Plans

U of U Health Plans 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

U of U Health Plans 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.

U of U Health Plans 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.

U of U Health Plans 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 are inappropriate to use because the description of those codes does not include identification of certain molecular alterations (i.e. SNVs, small (≤40 bp) and large (> 40 bp) indels, CNAs, and SVs) which are included in CGP testing.

2. Medicaid Plans

Coverage is determined by the State of Utah Medicaid program; if Utah State Medicaid has no published coverage position and InterQual criteria are not available, the U of U Health Plans Commercial criteria will apply. For the most up-to-date Medicaid policies

and coverage, please visit their website at: https://medicaid.utah.gov/utah-medicaid-official-publications/ or the Utah Medicaid code Look-Up tool

CPT/HCPCS codes covered by Utah State Medicaid may still require further evaluation to determine medical necessity for coverage.

Applicable Coding

CPT Codes

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

HCPCS Codes

No applicable codes

References:

1. Centers for Medicare and Medicaid Services. (October 9, 2017). "MolDX: Next Generation Sequencing Billing and Coding Guidelines" Article# A55624. CMS.gov. Accessed July 8, 2021. Available at: https://www.cms.gov/medicare-coverage-database/details/article-details.aspx?articleId=55624&ver=17&LCDId=38119&DocID=L38119&bc=gAAAAAgAIAAAAAAA&
2. Current Procedural Terminology (CPT®). (2021) –American Medical Association
3. National Cancer Institute. (2021) (NCI) NCI Dictionary of Genetic Terms "Next-Generation Sequencing" Available at: https://www.cancer.gov/publications/dictionaries/genetics-dictionary/def/next-generation-sequencing

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 it applies to an individual member.

U of U Health Plans makes no representations and accepts no liability with respect to the content of any external information cited or relied upon in this policy. U of U Health Plans updates its Coverage Policies regularly, and reserves the right to amend these policies and give notice in accordance with State and Federal requirements.