I. POLICY/CRITERIA

Coverage of multi-marker tumor panels using next generation sequencing in the diagnosis and treatment of cancer is available in the following circumstances:

A. Patients with the following conditions may be eligible for next-generation sequencing
   1. Patients newly diagnosed with stage IV non-small cell lung cancer (NSCLC).
   2. Patients newly diagnosed with cancer of unknown primary (CUP) or primary anatomic site.
   3. Patients with newly diagnosed hematologic malignancies with high frequencies of actionable mutations or limited treatment options in defined clinical care guidelines.
   4. Patients for whom tissue to perform evidence-based tumor genome mutation analysis is not available.
   5. Patients newly diagnosed with selected stage IV rare or uncommon solid tumors for whom very limited or no systemic treatment exists in clinical care guidelines and/or pathways.
   6. Patients newly diagnosed with selected Stage IV solid tumor types having poor prognosis, very limited benefit from standard of care chemotherapies and a high prevalence of actionable genomic alterations.
   7. Patients with stage IV solid tumors who have exhausted the established guideline-driven systemic therapy and requisite molecular testing but who desire further treatment.

B. General requirements

   All of the following conditions are met:
   1. Pathologic diagnosis consistent with categories A1-A7 above
   2. ECOG performance status 0-2
   3. Advance care planning (ACP) completed with a trained facilitator or a palliative care physician
   4. Submission by the treating physician of all pathology, imaging, and treatment notes as well as ACP consultation notes
   5. Service is requested from a contracted provider
C. Specific requirements

For the conditions A5-A7, patients must attest that they would be willing to consider participation in a clinical trial if the analysis identifies relevant clinical trials.

Requests for authorization should be submitted using the Next Generation Sequencing prior authorization form.

II. COVERAGE FOR DRUG THERAPY RECOMMENDED BY NEXT GENERATION SEQUENCING TESTS

Multi-marker tumor panels using next-generation sequencing analyses are intended to link actionable mutations with specific drugs to personalize therapy. While some mutations have known corresponding drug therapies in specific tumor types for may identify relevant clinical trials for which the patient may be eligible, these analyses will identify mutations for which there is insufficient evidence to confer coverage for a specific drug.

For example, targeted therapy for patients with melanoma who have a V600E BRAF mutation, several drugs have been shown to improve outcomes. However, for the same mutation in colon cancer, no benefit is realized and there are no FDA approved or NCCN recommended therapies.

Coverage for drug therapy recommended by next-gen sequencing results will be consistent with existing pharmacy coverage policy as outlined below.

A. To be covered, the prescribed drug(s) must meet one of the following three criteria:
   1. FDA approved indication
   2. Listing in one of the following drug compendium
      a. The American Hospital Formulary Service Drug Information
      b. Thomson Micromedex DrugDex or DrugPoints
      d. Clinical Pharmacology
   3. Provider submission of at least two peer-reviewed journal articles
      a. whose primary purpose is to evaluate the use of the drug for the off-label diagnosis for which it is requested, and
      b. that support the proposed off-label use as generally safe and effective for the patient's diagnosis. (Policy 11-0022 Documentation Required for Off-Label Use of Drugs)
B. In circumstances where the patient is eligible for a clinical trial, Priority Health will cover the cost of the clinical trial as outlined in the coverage policy *Clinical Trials - 91606*.

C. In all other circumstances, therapies recommended by next-generation sequencing testing either alone or in combination would not be covered, even under coverage policy *Experimental/Investigational/Unproven Care/Benefit Exceptions - 91117*. This coverage decision is consistent with The State of Michigan “Right to Try Act.”

Exception: For commercial members only, Priority Health would cover ongoing drug therapy with an experimental agent outside of a clinical trial if the patient:
1. successfully completes three months of drug therapy, **AND**
2. maintains performance status, **AND**
3. demonstrates either
   a. a clinically significant reduction in a relevant tumor biomarker during that time, **OR**
   b. at least partial tumor regression by RECIST criteria ([http://www.recist.com/index.html](http://www.recist.com/index.html)) or by Immune-Related Response Criteria ([http://clincancerres.aacrjournals.org/content/15/23/7412.long](http://clincancerres.aacrjournals.org/content/15/23/7412.long))

There are no exceptions for Medicare beneficiaries. However, beneficiaries have the right to appeal any denial.

### III. MEDICAL NECESSITY REVIEW

- [ ] Required  
- [ ] Not Required  
- [ ] Not Applicable  

- All tests performed at non-participating laboratories will require prior authorization for all products.

### IV. APPLICATION TO PRODUCTS

Coverage is subject to member’s specific benefits. Group specific policy will supersede this policy when applicable.

- **HMO/EPO:** *This policy applies to insured HMO/EPO plans.*
- **POS:** *This policy applies to insured POS plans.*
- **PPO:** *This policy applies to insured PPO plans. Consult individual plan documents as state mandated benefits may apply. If there is a conflict between this policy and a plan document, the provisions of the plan document will govern.*
V. BACKGROUND

At present (2014), next-generation sequencing of patient tumors to personalize cancer treatment has only been endorsed by the National Comprehensive Cancer Network (NCCN) for non-small cell lung cancer. However, several factors are converging that warrant reconsideration of this standard in selected patients and selected tumor types outlined in this policy. First, the Accountable Care Act requires health plans to cover phase 1 through phase 4 clinical trials. Second, the NCCN recommends clinical trials as the standard of care even when other options exist. Third, as noted above, eligibility for ACA-eligible cancer clinical trials is often determined by emerging biomarkers. Fourth there and most importantly, for certain malignancies there remains a high unmet need and limited therapeutic options. In the circumstances outlined in this policy, Priority Health will cover next generation sequencing to provide additional insights into the therapeutic options available to patients and their physicians.

VI. CODING INFORMATION

ICD-10 Codes: not specified

CPT/HCPCS Codes:
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 (Not covered for Medicaid)
81455 Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm, DNA and RNA analysis when performed, 51 or greater genes (e.g., ALK, BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MLL, NPM1, NRAS, MET, NOTCH1, PDGFRα, PDGFRβ, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed  (Not covered for Medicaid)

0008M Oncology (breast), mRNA analysis of 58 genes using hybrid capture, on formalin-fixed paraffin-embedded (FFPE) tissue, prognostic algorithm reported as a risk score   (Not covered for Medicaid)

Not Covered:

81445 Targeted genomic sequence analysis panel, solid organ neoplasm, DNA analysis and RNA analysis when performed, 5-50 genes (e.g., ALK, BRAF, CDKN2A, EGFR, ERBB2, KIT, KRAS, NRAS, MET, PDGFRα, PDGFRβ, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed

81525 Oncology (colon), mRNA, gene expression profiling by real-time RT-PCR of 12 genes (7 content and 5 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a recurrence score (OncotypeDx® Colon Cancer Assay)

0006M Oncology (hepatic), mRNA expression levels of 161 genes, utilizing fresh hepatocellular carcinoma tumor tissue, with alpha-fetoprotein level, algorithm reported as a risk classifier (HeproDx®)

VII. REFERENCES


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All Current Procedure Terminology (CPT) codes, descriptions, and other data are copyrighted by the American Medical Association.

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Priority Health’s medical policies are intended to serve as a resource to the plan. They are not intended to limit the plan’s ability to interpret plan language as deemed appropriate. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment they choose to provide.

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