FORCE
Facing Hereditary Cancer EMPOWERED

November 12, 2021

National Government Services
Medical Policy Unit
P.O. Box 7108
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Submitted electronically to: PartBLCDComments@anthem.com

RE: Proposed LCD - Genomic Sequence Analysis Panels in the Treatment of Solid Organ Neoplasms (DL37810)

To Whom it May Concern:

FORCE (Facing Our Risk of Cancer Empowered) is the only national nonprofit organization representing people and families affected by hereditary cancers. Our programs provide education, support, advocacy, and research to empower this community to make informed decisions about their health, including decisions surrounding genetic/genomic testing and targeted therapies. We are pleased to submit the following comments on behalf of our constituents in the states that fall within the National Government Services, Inc. Medicare region.

Recent advancements in genetic and genomic sequencing have changed the landscape for cancer treatment, significantly improving patient care, quality of life, and outcomes. As noted in the Local Coverage Determination (LCD), Comprehensive Genomic Profile (CGP) Testing is a "NGS approach that uses a single assay to assess hundreds of genes including relevant cancer biomarkers, with solid evidentiary support for clinical utility in guidelines and clinical trials." CGP has become the standard of care in oncology. Unfortunately, Medicare beneficiaries in the National Government Services region, encompassing 10 states, have not had access to these tests, which may inform use of an effective versus ineffective treatment—potentially making the difference between life and death.

FORCE applauds National Government Services for the proposed coverage of NGS CGP. This policy will expand access and more closely align with reimbursement policies under other Medicare Administrative Contractors. To improve the coverage provided under this LCD, we recommend the following revisions to help ensure broad, equitable access to NGS CGP tests.

1. **LCD focus on "advanced somatic cancers"**

   The proposed policy's focus on somatic genetic mutations is short-sighted, failing to acknowledge that some mutations found in somatic CGP testing may, in fact, be germline in nature (i.e., BRCA1 and BRCA2). In certain circumstances, the standard of care for cancer driven by a germline mutation will differ from that of a cancer with somatic genetic alterations, so it is important to test for and distinguish between the two.

With current technologies and therapeutic options, germline testing may be needed to ensure appropriate treatment of metastatic cancer. A recent study in the *Journal of Clinical Oncology* found that 10% of metastatic cancers have an underlying, actionable germline mutation and 4% were Level 1 (linked to an approved-FDA drug treatment for their cancer). In addition, 71% of patients in this study did not know they had an inherited genetic mutation; this knowledge might have allowed for earlier diagnoses, when the cancer was more easily treated, or guided treatment of their metastatic disease.[i]

Proposed LCD DL37810 references CMS NCD 90.2, which provides for coverage of Next Generation Sequencing at the national level. This NCD also initially failed to recognize the clinical utility of germline testing. Ultimately, a revised NCD was published, distinguishing between somatic and germline testing with separate sections in the NCD language—acknowledging the value of each in treatment of advanced cancers.

Recommendation:

- Revise the proposed LCD to include germline testing, recognizing its potential need and value as a tool in determining appropriate treatment for certain advanced cancers.

2. **"CGP NGS testing for patients with advanced cancer is reasonable and necessary only when more limited (e.g., individual analyte or targeted panel (5-50 genes) testing is insufficient"**

   This language would create a requirement that potentially inadequate small gene panels must be utilized prior to comprehensive NGS CGP, preventing immediate access to more thorough testing approaches. As noted in the proposed LCD section on NGS CGP, the "decreasing cost and proliferation of actionable biomarkers" justifies access to broader panels and expedites access to the most appropriate care.

   Recommendations:

   - Eliminate this language/prerequisite from the LCD.
   - If National Government Services choose to retain the stated prerequisite, we ask that it clearly defines when larger panels are considered reasonable and necessary.

3. **The patient has "not been previously tested with a CGP for the same cancer genetic content"**

   It is unclear whether the term "cancer genetic content" refers to the genetic content of the tumor specimen or the genetic content of the sequencing panel. Limiting access to retesting via NGS CGP for the same cancer genetic content can miss assessments of tumor heterogeneity or clonal evolution, which may be critical information for therapeutic or prognostic purposes. Additionally, it is not uncommon for a tumor to evolve in response to treatment or over time. Clinical guidelines recommend retesting tumors upon progression to evaluate resistance mutations and identify new therapeutic targets.

   It is also important to note that that NGS CGP has the potential to identify one or more relevant germline genetic mutations that changes medical management, including surgical and treatment decisions as well as screening for additional cancers. As such, further testing may be indicated to determine if these mutations are somatic or germline.

Recommendations:

- Clarify the "same genetic content" language to permit use of the same NGS CGP to test different tissue samples.
- Make clear that this condition allows follow-up or repeat testing when:
  a) a CGP test may provide additional genetic information not previously tested for or obtained, or
  b) there is reason to believe that the genetic content may have changed (e.g., progression from primary tumor to more advanced disease or metastasis or a tumor is initially sensitive to treatment but becomes resistant over time).

3. **"Testing assays must be FDA approved, or if a laboratory developed test (LDT), have published, peer-reviewed studies supporting analytic validity."**

   How many "published, peer-reviewed studies" are required? This language may create an unreasonable burden, which ultimately will limit patient access to quality, evidence-based NGS CGP tests. The majority of LDTs are not FDA approved. An evidentiary standard of multiple published, peer-reviewed studies in lieu of FDA approval sets the bar too high because most journals are not interested in publishing articles on NGS test data, especially if the data parallel previously published articles.

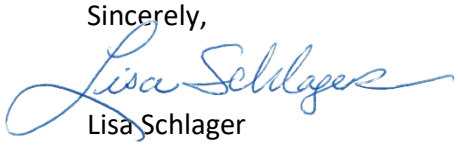
   The New York State Department of Health's Clinical Laboratory Evaluation Program (CLEP) is well-regarded for its rigorous standards, serving as a benchmark for validating the analytical performance of NGS-based LDTs. The Wadsworth Center, where CLEP is based, has FDA accreditation as a third-party reviewer for premarket notifications for NGS-based CGPs. Many NGS CGP tests undergo evaluation for approval by CLEP, ensuring high-quality, accurate analytical validity and clinical performance.

   Recommendations:

   - Add language to include NGS CGP tests that have been approved by the New York State Department of Health.
   - Clarify that a single peer-reviewed study is adequate to meet the evidentiary standard for coverage of an NGS CGP test under this LCD.

At a time when our country is moving to embrace and realize the value of precision medicine, we should strive to ensure that individuals diagnosed with cancer have access to the right test at the right time. National Government Services' proposed LCD "Genomic Sequence Analysis Panels in the Treatment of Solid Organ Neoplasms" strives to align its Medicare coverage with the existing standard-of-care; this is a positive move for all involved. Thank you for your consideration of our comments.

Sincerely,



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[i] Stadler ZK, Maio A, Chakaravarty D, et al. Therapeutic Implications of Germline Testing in Patients With Advanced Cancers. Journal of Clinical Oncology. 2021; 39(24): 2698-2709. Published online June 16, 2021.