Geisinger

Geisinger Health Plan Policies and Procedure Manual

Policy: MP246

Section: Medical Benefit Policy

Subject: Multi-gene Expression Assay for Predicting Recurrence in Colon Cancer

Applicable Lines of Business

Commercial	**X**	**CHIP**	**X**
Medicare	**X**	**ACA**	**X**
Medicaid	**X**		

I. Policy: Multi-gene Expression Assay for Predicting Recurrence in Colon Cancer

II. Purpose/Objective:

To provide a policy of coverage regarding Multi-gene Expression Assay for Predicting Recurrence in Colon Cancer

III. Responsibility:

A. Medical Directors

B. Medical Management Department

IV. Required Definitions

1. Attachment – a supporting document that is developed and maintained by the policy writer or department requiring/authoring the policy.
2. Exhibit – a supporting document developed and maintained in a department other than the department requiring/authoring the policy.
3. Devised – the date the policy was implemented.
4. Revised – the date of every revision to the policy, including typographical and grammatical changes.
5. Reviewed – the date documenting the annual review if the policy has no revisions necessary.

V. Additional Definitions

Medical Necessity or Medically Necessary means Covered Services rendered by a Health Care Provider that the Plan determines are:

a. appropriate for the symptoms and diagnosis or treatment of the Member's condition, illness, disease or injury;
b. provided for the diagnosis, and the direct care and treatment of the Member's condition, illness disease or injury;
c. in accordance with current standards of good medical treatment practiced by the general medical community;
d. not primarily for the convenience of the Member, or the Member's Health Care Provider; and the most appropriate source or level of service that can safely be provided to the Member. When applied to hospitalization, this further means that the Member requires acute care as an inpatient due to the nature of the services rendered or the Member's condition, and the Member cannot receive safe or adequate care as an outpatient.

Medicaid Business Segment

Medically Necessary — A service, item, procedure, or level of care that is necessary for the proper treatment or management of an illness, injury, or disability is one that:

- Will, or is reasonably expected to, prevent the onset of an illness, condition, injury or disability.

- Will, or is reasonably expected to, reduce or ameliorate the physical, mental or developmental effects of an illness, condition, injury or disability.
- Will assist the Member to achieve or maintain maximum functional capacity in performing daily activities, taking into account both the functional capacity of the Member and those functional capacities that are appropriate for Members of the same age

DESCRIPTION:
In early -stage disease, residual circulating tumor DNA (ctDNA) is released from cancer cells, after definitive local therapy and, is indicative of molecular residual disease (MRD). The presence of MRD can be used to identify patients at highest risk of recurrent or metastatic disease. In turn, individuals with no identifiable MRD may be candidates for de-escalation approaches, given the associated favorable prognosis.

Oncotype DX® Colon Cancer Test is a 12-gene expression test designed to predict the likelihood of disease recurrence for stage II colon cancer patients following surgery. Gene expression is quantified from microdissected fixed paraffin-embedded primary colon cancer tissue. The level of expression of the prognosis and predictive signature are then reported as a recurrence score.

Signatera is a personalized molecular residual disease assay (MRD) using circulating tumor DNA (ctDNA), paired with a matched normal tissue sample that is designed ~~for each patient to help~~ to identify relapse of disease. The Signatera test is tumor-informed and filters CHIP-related variants to be filtered out to decrease the rate of false positive findings. Signatera can also be used for longitudinal disease monitoring; please reference MP360 “Minimal Residual Disease NGS Testing”.

INDICATIONS: <u>Requires Prior Medical Director or designee Authorization</u>

For the Commercial Business Segments

The Plan considers Oncotype DX™colon assay or Signatera as medically necessary to assess the need for adjuvant chemotherapy in newly diagnosed colon cancer when ALL of the following are met:

- Diagnosis of Stage II colon cancer is made; and
- Member has undergone initial surgical resection; and
- Provider and member are committed to utilize the recurrence risk score to guide the treatment plan

For the Medicare and Medicaid Business Segments – Although there is no National Coverage Determination issued for this service, CMS directives may allow this testing to be considered for coverage when used to predict risk of recurrence risk in patients with stage II colon cancer. Effective Sept 18, 2011, Palmetto GBA established a formal coverage policy for all Medicare patients. This local carrier determination is applicable nationally. Please refer to policy number A51725 on Centers for Medicare & Medicaid Services website.

Although there is no National Coverage Determination issued for this service, CMS directives may allow Signatera testing to be considered for coverage when used to predict risk of recurrence risk in patients with colon cancer. Effective 12/26/2021 Palmetto GBA established a formal coverage policy for all Medicare patients. This local carrier determination is applicable nationally. Please refer to policy number A58376 on Centers for Medicare & Medicaid Services website. Coverage criteria under the policy have been met for (1) the diagnosis of disease progression, recurrence, or relapse for colon cancer and (2) monitoring of response to immune-checkpoint inhibitor therapy for any solid tumor.

Medicaid Business Segment:
Any requests for services that do not meet criteria set in the PARP may be evaluated on a case by case basis

CODING ASSOCIATED WITH: Oncotype Dx - Multi-gene Expression Assay for Predicting Recurrence in Colon Cancer
The following codes are included below for informational purposes and may not be all inclusive. Inclusion of a procedure or device code(s) does not constitute or imply coverage nor does it imply or guarantee provider reimbursement. Coverage is determined by the member specific benefit plan document and any applicable laws regarding coverage of specific services. Please note that per Medicare coverage rules, only specific CPT/HCPCS Codes may be covered for the Medicare Business Segment. Please consult the CMS website at www.cms.gov or the local Medicare Administrative Carrier (MAC) for more information on Medicare coverage and coding requirements

81445 Targeted genomic sequence 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. *{Signatera}*
81479 Unlisted molecular pathology procedure
81525 Oncology (colon), MRNA, gene expression profiling by real-time R-PCR of 12 genes (7 context and 5 housekeeping), utilizing formalin-fixed paraffin embedded tissue, algorithm reported as a recurrence score) *{Oncotype DX® Colon Cancer Test}*

LINE OF BUSINESS:
Eligibility and contract specific benefits, limitations and/or exclusions will apply. Coverage statements found in the line of business specific benefit document will supersede this policy. For Medicare, applicable LCD's and NCD's will supercede this policy. For PA Medicaid Business segment, this policy applies as written.

REFERENCES:
O'Connell MJ, Lavery IC, Gray RG, et al. Comparison of molecular and pathologic features of stage II and stage III colon cancer in four large studies conducted for development of the 12-gene colon cancer recurrence score. American Society of Clinical Oncology Gastrointestinal Cancers Symposium, 2010, Abstract 280.

Rosenberg R, Maak M, Nitsche U, et al. Independent validation of a prognostic genomic profile (ColoPrint) for stage II colon cancer (CC) patients. American Society of Clinical Oncology Gastrointestinal Cancers Symposium, 2010, Abstract 3513.

Salazar R, Marshall J, Stork-Sloots L, et al. The PARSC trial, a prospective study for the assessment of recurrence risk in stage II colon cancer (CC) patients using ColoPrint. American Society of Clinical Oncology Gastrointestinal Cancers Symposium, 2010, Abstract TPS199.

Meropol NJ, Lyman GH, Chien R, et al. Use of a multigene prognostic assay for selection of adjuvant chemotherapy in patients with stage II colon cancer: Impact on quality-adjusted life expectancy and costs. American Society of Clincical Oncology Gastrointestinal Cancers Symposium, 2011, Abstract 491

Webber EM, Lin JS, Whitlock EP, Oncotype DX tumor gene expression profiling in stage II colon cancer. PLoS Curr. September 2010, 2(2) PMCID: PMC2940137

Gray RG, Quirke P, Handley K et al. Validation study of a quantitative multigene reverse transcriptase-polymerase chain reaction assay for assessment of recurrence risk in patients with stage II colon cancer. J.Clin Oncology. 2011; 29(35):4611-9.

Colon Cancer: Third Successful Prospectively Designed Study of Oncotype DX Colon Cancer Test In Patients with Stage II Disease, First Validation Study in Patients with Stage III Disease (Abstract #3512); Separate Study Demonstrates 29 percent Change in Treatment Recommendations in Stage II Colon Cancer Patients (Abstract #3626)

Clark-Langone KM, Sangli C, Krishnakumar J, Watson D. Translating tumor biology into personalized treatment planning: analytical performance characteristics of the Oncotype DX Colon Cancer Assay. BMC Cancer 2010;10:691

O'Connell MJ, Lavery I, Yothers G, et al. Relationship between tumor gene expression and recurrence in four independent studies of patients with stage II/III colon cancer treated with surgery alone or surgery plus adjuvant fluorouracil plus leucovorin. J Clin Oncol 2010;28:3937-44.

Lavery I, Hammel J, Cowens J, et al. Relationship between tumor gene expression and recurrence in an observational cohort of patients with stage II/III colon cancer treated with surgery only: Quantitative RT-PCR assay of 375 genes in fixed paraffin-embedded (FPE) tissue. Abstract no. 302. In: Gastrointestinal Cancers Symposium. Orlando, FL; 2008

O'Connell MJ, Yothers G, Paik S, et al. Relationship between tumor gene expression and recurrence in patients with stage II/III colon cancer treated with surgery + 5-FU/LV in NSABP C-06: Consistency of results with two other independent studies. Abstract no. 301. In: Gastrointestinal Cancers Symposium. Orlando, FL; 2008.

Clark-Langone KM, Wu JY, Sangli C, et al. Biomarker discovery for colon cancer using a 761 gene RT-PCR assay. BMC Genomics 2007;8:279.

Schwartzberg L, Babkowski R. Oncotype DX assay for predicting recurrence of stage II colon cancer Community Oncology 2010;7:198-201

Midgley R, Rasul K, Al Salama H, Kerr DJ. Gene profiling in early stage disease. Cancer J 2010;16:210-213

Breener B, Geva R, Rothney M, et. al. Impact of the 12-gene colon assay on clinical decision making for adjuvant therapy in stage II colon cancer patients. Value Health. Jan 2016;19(1):82-87. PMID 26797240

UpToDate. Pathology and Prognostic Determinants of Colorectal Cancer. Carolyn C. Compton M.D., PhD. Topic last updated February 1, 2019

NCCN Clinical Practice Guidelines in Oncology. National Comprehensive Cancer Network, Inc. Colon Cancer. v2.2023

Symonds EL, Pedersen SK, Murray D, et al. Circulating epigenetic biomarkers for detection of recurrent colorectal cancer. Cancer. Apr 01 2020; 126(7): 1460-1469.

Oki E, Watanabe J, Sato T, et al. Impact of the 12-gene recurrence score assay on deciding adjuvant chemotherapy for stage II and IIIA/B colon cancer: the SUNRISE-DI study. ESMO Open. Jun 2021; 6(3): 100146

Tie J, Wang Y, Tomasetti C, et al. Circulating tumor DNA analysis detects minimal residual disease and predicts recurrence in patients with stage II colon cancer. Sci Transl Med. 2016 Jul 6;8(346):346ra92. PMID: 27384348.

Malla M, Loree JM, Kasi PM, Parikh AR. Using Circulating Tumor DNA in Colorectal Cancer: Current and Evolving Practices. J Clin Oncol. 2022 Aug 20;40(24):2846-2857. PMID: 35839443.

This policy will be revised as necessary and reviewed no less than annually.

Devised: 11/2010

Revised: 2/12 (CMS mandate), 7/12 (criteria), 8/12 (exclusions removed and Medicare info added); 7/22 (add Medicare coverage info); 7/23 (add Commercial header)

Reviewed: 11/11**,** 8/13, 8/14; 8/15, 7/16, 7/17, 6/18, 7/19, 7/20, 7/21,