Medical Coverage Policy | Gene Expression Profile Testing and Circulating Tumor DNA Testing for Predicting Recurrence in Colon Cancer

EFFECTIVE DATE: 01|01|2024
POLICY LAST REVIEWED: 09|06|2023

OVERVIEW

Gene expression profile (GEP) and circulating tumor DNA (ctDNA) tests have been developed for use as prognostic markers of stage II or III colon cancer to help identify patients who are at high-risk for recurrent disease and could be candidates for adjuvant chemotherapy.

This policy addresses the following test(s):

- Oncotype DX® Colon (Genomic Health) CPT code 81525

MEDICAL CRITERIA

Not applicable

PRIOR AUTHORIZATION

Not applicable

POLICY STATEMENT

Medicare Advantage Plans and Commercial Products

The following gene expression profile (GEP) and circulating tumor DNA (ctDNA) test(s) for the prognostic markers of stage II or III colon cancer following surgery may be considered medically necessary for the following test(s):

- Oncotype DX® Colon (Genomic Health)

Note: Laboratories are not allowed to obtain clinical authorization or participate in the authorization process on behalf of the ordering physician. Only the ordering physician shall be involved in the authorization, appeal or other administrative processes related to prior authorization/medical necessity.

In no circumstance shall a laboratory or a physician/provider use a representative of a laboratory or anyone with a relationship to a laboratory and/or a third party to obtain authorization on behalf of the ordering physician, to facilitate any portion of the authorization process or any subsequent appeal of a claim where the authorization process was not followed and/or a denial for clinical appropriateness was issued, including any element of the preparation of necessary documentation of clinical appropriateness. If a laboratory or a third party is found to be supporting any portion of the authorization process, BCBSRI will deem the action a violation of this policy and severe action will be taken up to and including termination from the BCBSRI provider network. If a laboratory provides a laboratory service that has not been authorized, the service will be denied as the financial liability of the participating laboratory and may not be billed to the member.

Commercial Products

Some genetic testing services are not covered and a contract exclusion for any self-funded group that has excluded the expanded coverage of biomarker testing related to the state mandate, R.I.G.L. §27-19-81 described in the Biomarker Testing Mandate policy. For these groups, a list of which genetic testing services are covered with prior authorization, are not medically necessary or are not covered because they are a contract exclusion can be found in the Coding section of the Genetic Testing Services or Proprietary Laboratory Analyses policies. Please refer to the appropriate Benefit Booklet to determine whether the member's plan has customized benefit coverage. Please refer to the list of Related Policies for more information.

COVERAGE

Benefits may vary between groups and contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage or Subscriber Agreement for applicable benefits/coverage

BACKGROUND

Colon Cancer

According to estimates by the National Cancer Institute, in 2022 over 151,000 new cases of colorectal cancer will be diagnosed in the U.S., and nearly 53,000 people will die of this cancer. Five-year survival estimates are around 65%. Disparities in colorectal cancer outcomes have been identified in different subgroup classifications based on race and ethnicity, age, socioeconomic status, insurance access, geography, and environmental exposures. For example, in the U.S. between 2012- 2016, mortality rates were highest amongst non-Hispanic Black patients (incidence rate of 45.7 per 100,000), which were 20% and 50% higher than rates amongst non-Hispanic White and Asian patients, respectively. Additionally, non-Hispanic Black patients may have limited opportunities for therapeutic interventions due to experiencing higher inequities in comorbidities.

Colorectal cancer is classified as stage II (also called Dukes B) when it has spread outside the colon and/or rectum to nearby tissue but is not detectable in lymph nodes (stage III disease, also called Dukes C) and has not metastasized to distant sites (stage IV disease). Primary treatment is surgical resection of the primary cancer and colonic anastomosis. After surgery, the prognosis is good, with survival rates of 75% to 80% at 5 years. A Cochrane review by Figueredo et al (2008), assessing 50 studies of adjuvant therapy versus surgery alone in stage II patients, found a small though statistically significant absolute benefit of chemotherapy for disease-free survival but not for overall survival. Therefore, adjuvant chemotherapy with 5-fluorouracil (5-FU), capecitabine, CAPEOX (capecitabine and oxaliplatin), or FOLFOX (5-FU and oxaliplatin) is recommended only for resected patients with high-risk stage II disease (ie, those with poor prognostic features).

However, the clinical and pathologic features used to identify high-risk disease are not well-established, and patients for whom benefits of adjuvant chemotherapy would most likely outweigh harms cannot be identified with certainty. The current diagnostic system relies on a variety of factors, including tumor substage IIB (T4a tumors that invade the muscularis propria and extend into the surface of the visceral peritoneum) or IIC (T4b tumors that invade or are adherent to other organs or structures), obstruction or bowel perforation at initial diagnosis, an inadequately low number of sampled lymph nodes at surgery (< 12), histologic features of aggressiveness, and indeterminate or positive resection margins. Gene expression profiling and circulating tumor DNA (ctDNA) tests are intended to facilitate identifying stage II patients most likely to experience recurrence after surgery and most likely to benefit from additional treatment.

Of interest, a review by Vilar and Gruber (2010) has noted that microsatellite instability and mismatch repair deficiency in colon cancer may represent confounding factors to be considered in treatment. These factors may identify a minority (15% to 20%) of the population with improved disease-free survival who may derive no benefit or may exhibit deleterious effects from adjuvant 5-FU plus leucovorin-based treatments. Patient microsatellite instability and mismatch repair status may be critically important in how to study, interpret, and use a particular gene expression profile test.

Regulatory Status

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments (CLIA). Multigene expression assay testing and ctDNA testing for predicting recurrent colon cancer is available under the auspices of CLIA. Laboratories that offer laboratory-developed tests must be licensed by the CLIA for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.

Gene expression profile and ctDNA tests for colon cancer currently commercially available include:

- Oncotype DX® Colon (Genomic Health)

CODING

Medicare Advantage Plans and Commercial Products
The following CPT code is medically necessary for Medicare Advantage Plans and Commercial Products when filed with an ICD-10 diagnosis code(s)* listed below:

The following CPT code(s) can be used for Oncotype DX® Colon:
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

***ICD-10 diagnosis code(s)**
C18.0-C20
C21.1

RELATED POLICIES

Biomarker Testing Mandate
Genetic Testing Services

PUBLISHED

Provider Update, November 2023

REFERENCES

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