October 31st, 2017

Medical Policy

Multigene Expression Assay for Predicting Recurrence in Colon Cancer

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Policy Number: 239
BCBSA Reference Number: 2.04.61
NCD/LCD: N/A
Oncotype DX Colon Cancer Assay Coding and Billing Guidelines (M0002, V15)

Related Policies
None

Policy
Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity

Gene expression assays for determining the prognosis of stage 2 or stage 3 colon cancer following surgery are considered INVESTIGATIONAL.

Medicare HMO BlueSM and Medicare PPO BlueSM Members

Coding guidance for Medicare Advantage members living in Massachusetts or Medicare Advantage members living outside of Massachusetts can be found through the link below.

Oncotype DX Colon Cancer Assay Coding and Billing Guidelines (M0002, V15)

For medical necessity criteria and coding guidance for Medicare Advantage members living outside of Massachusetts, please see the Centers for Medicare and Medicaid Services website for information regarding your specific jurisdiction at https://www.cms.gov.

Prior Authorization Information
Pre-service approval is required for all inpatient services for all products. See below for situations where prior authorization may be required or may not be required.
Yes indicates that prior authorization is required.
No indicates that prior authorization is not required.
N/A indicates that this service is primarily performed in an inpatient setting.
Outpatient Coverage

<table>
<thead>
<tr>
<th>Plan Type</th>
<th>Coverage Details</th>
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<tbody>
<tr>
<td>Commercial Managed Care (HMO and POS)</td>
<td>This is not a covered service.</td>
</tr>
<tr>
<td>Commercial PPO and Indemnity</td>
<td>This is not a covered service.</td>
</tr>
<tr>
<td>Medicare HMO Blue℠</td>
<td>No</td>
</tr>
<tr>
<td>Medicare PPO Blue℠</td>
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CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

The following CPT codes are considered investigational for Commercial Members: Managed Care (HMO and POS), PPO and Indemnity:

### CPT Codes

<table>
<thead>
<tr>
<th>CPT codes:</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>81525</td>
<td>Oncology (colon), mmrna, 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</td>
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</tbody>
</table>

Description

Of patients with stage 2 colon cancer, 75% to 80% are cured by surgery alone, and the absolute benefit of chemotherapy for the overall patient population is small. Patients most likely to benefit from chemotherapy are difficult to identify by standard clinical and pathologic risk factors. Genomic tests are intended to be used as an aid for identifying stage 2 patients most likely to experience recurrence after surgery and most likely to benefit from additional treatment.

Colorectal cancer is classified as stage 2 (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 3 disease, also called Dukes C) and has not metastasized to distant sites (stage 4 disease). Primary treatment is surgical resection of the primary cancer and colonic anastomosis. After surgery prognosis is good, with survival rates of 75% to 80% at 5 years. A 2008 meta-analysis of 50 studies of adjuvant therapy versus surgery alone in stage 2 patients found statistically significant, although small, absolute benefit of chemotherapy for disease-free survival (DFS) but not for overall survival.

Therefore, adjuvant chemotherapy with 5-fluorouracil or capecitabine is recommended only as an option for resected patients with high-risk stage 2 disease (ie, those with poor prognostic features). However, 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 system relies on a variety of factors, including tumor substage 2B (T4A tumors that invade the muscularis propria and extend into pericolorectal tissues) or 2C (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, a high preoperative carcinoembryonic antigen level, and indeterminate or positive resection margins.

For patients with stage 3 colon cancer, current guidelines from the National Comprehensive Cancer Network recommend “6 months of adjuvant chemotherapy after primary surgical treatment. However, some have questioned the benefit of adjuvant chemotherapy in subsets of patients with stage 3 disease.
(eg, stage 3A) whose predicted survival may actually exceed that of some stage 2 patients (eg, stage 2C).

Of interest, a recent review has noted that microsatellite instability (MSI) and mismatch repair (MMR) deficiency in colon cancer may represent confounding factors to be considered in treatment. These factors may identify a small proportion (15%-20%) of the population with improved DFS who may derive no benefit or may exhibit deleterious effects from adjuvant fluorouracil/leucovorin-based treatments. Patient MSI and MMR status may be critically important in how to study, interpret, and use a particular GEP test.

Summary
Gene expression profiling (GEP) tests have been developed and reported for use as prognostic markers in stage 2 or stage 3 colon cancer to help identify patients who are at high risk for recurrent disease and could be candidates for adjuvant chemotherapy.

The evidence for the use of GEP tests in patients who have stage 2 or stage 3 colon cancer includes development and validation studies. Relevant outcomes are disease-specific survival, test accuracy, test validity, and change in disease status. The available evidence indicates that GEP tests for colon cancer can improve risk prediction, particularly the risk of recurrence in patients with stage 2 or stage 3 colon cancer. However, evidence to date is insufficient to permit conclusions on how GEP classification compares with other approaches for identifying recurrence risk in stage 2 or stage 3 patients, or on how GEP classification impacts patient outcomes (clinical utility). There is even less evidence to permit conclusions about how GEP classification compares with other approaches for management of other stages of colon cancer. The evidence is insufficient to determine the effects of the technology on health outcomes.

Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
</tr>
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<tbody>
<tr>
<td>9/2017</td>
<td>New references added from BCBSA National medical policy.</td>
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<tr>
<td>10/2016</td>
<td>New references added from BCBSA National medical policy.</td>
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<tr>
<td>6/2015</td>
<td>Local Coverage Determination (LCD): Molecular Diagnostic Tests (MDT) (L33541) added.</td>
</tr>
<tr>
<td>10/2014</td>
<td>New references added from BCBSA National medical policy.</td>
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<td>12/2013</td>
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<tr>
<td>2/2013</td>
<td>New references from BCBSA National medical policy.</td>
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Information Pertaining to All Blue Cross Blue Shield Medical Policies
Click on any of the following terms to access the relevant information:
- Medical Policy Terms of Use
- Managed Care Guidelines
- Indemnity/PPO Guidelines
- Clinical Exception Process
- Medical Technology Assessment Guidelines
References


