Protocol

Multigene Expression Assay for Predicting Recurrence in Colon Cancer

(20461)

Medical Benefit		**Effective Date**: 10/01/13	**Next Review Date**: 07/15
Preauthorization	No	**Review Dates**: 09/10, 07/11, 07/12, 07/13, 07/14	

The following Protocol contains medical necessity criteria that apply for this service. It is applicable to Medicare Advantage products unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. ***Preauthorization is not required but is recommended if, despite this Protocol position, you feel this service is medically necessary.*** *Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.*

Description

Over a dozen different gene expression profile (GEP) tests have been developed and reported for use as prognostic markers in stage II colon cancer. These assays are intended to help identify patients with stage II colon cancer who are at high risk for recurrent disease and would be good candidates for adjuvant chemotherapy. Five assays are currently being marketed for clinical use in the United States: ColonPRS®, Signal Genetics, New York, NY; Coloprint® Agendia NV, Amsterdam, Netherlands; Genefx Colon®, Precision Therapeutics, Pittsburgh, PA; OncoDefender™-CRC (colon and rectal cancer), Everist Genomics, Ann Arbor, MI; and Oncotype DX® colon cancer test, Genomic Health, Inc., Redwood City, CA. The gene signatures range from as small as five to as many as 634 genes. Independent validation studies ranging in size from 33 to 1,436 patients have been reported on these assays.

Background

Of patients with stage II colon cancer, 75–80% are cured by surgery alone, and the absolute benefit of chemotherapy for the patient population is small. Those patients who are 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 in identifying those stage II patients most likely to experience recurrence after surgery. They are also intended to identify those patients most likely to benefit from additional treatment.

Colorectal cancer is classified stage II when it has spread outside the colon and/or rectum to nearby tissue but is not detectable in the lymph nodes and has not metastasized to distant sites (also called Dukes B). The 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 five years. (1) Meta-analysis of several trials of adjuvant therapy versus surgery alone in all stage II patients found statistically significant, although small, absolute benefit of chemotherapy for disease-free survival but not for overall survival. (1) Therefore, adjuvant chemotherapy with 5-fluorouracil (5-FU) or capecitabine is recommended only as an option for resected patients with high-risk stage II disease (i.e., those with poor prognostic features). (2) However, the clinical and pathologic features used to identify high-risk disease are not well-established, and the patients for whom the benefits of adjuvant chemotherapy would most likely outweigh the harms cannot be identified with certainty. The current system relies on the use of a variety of factors including tumor sub-stage IIB (T4A tumors that invade the muscularis propria and extend into pericolorectal tissues) or IIC (T4B tumors that invade or are adherent to other organs or structures), obstruction or bowel perforation at initial diagnosis, inadequately low number of sampled lymph nodes at surgery (12 or less); histological features of aggressiveness, a high preoperative carcinoembryonic antigen level, and the presence of indeterminate or positive resection margins. (2)

Of interest, a recent review has noted that microsatellite instability and mismatch repair (MMR) deficiency in colon cancer may represent confounding factors to be considered in treatment. (3) The finding of these factors may identify a small population (15% to 20%) of the population with improved disease-free survival who may derive no benefit or may exhibit deleterious effects from adjuvant fluorouracil/leucovorin-based treatments. The status of patients with regard to these findings may be critically important in how to study, interpret, and use a particular GEP test.

Regulatory Status

To date, no gene expression test for evaluation of prognosis in stage II colon cancer has been cleared for marketing by the U.S. Food and Drug Administration (FDA). These tests are offered as laboratory-developed assays in Clinical Laboratory Improvement Amendment (CLIA)-licensed laboratories operated by each company and currently do not require FDA premarket review as a result of enforcement discretion.

Policy (Formerly Corporate Medical Guideline)

Gene expression assays for determining the prognosis of stage II colon cancer following surgery are considered **investigational**.

Medicare Advantage

The Oncotype DX® colon cancer test may be considered **medically necessary** when used to determine prognosis and determine the treatment plan.

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this Protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

References

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

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23. Noridian Administrative Services, LLC Local Coverage Determination (LCD): Molecular Diagnostic Tests (MDT) (L33541), Primary Geographic Jurisdiction-Northern, California, Revision Effective Date For services performed on or after 09/16/2013.