Gene Expression Profiling for the Management of Breast Cancer

Descriptive Narrative

Clinical features that guide decision to use chemotherapy
Most instances of estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-negative breast cancer <1 cm in size, and all cancers ≤0.5 cm in size, have a good prognosis with endocrine therapy alone, and do not typically require adjuvant chemotherapy. At the other end of the risk spectrum, most women with stage III breast cancers will warrant adjuvant chemotherapy because of their risk of recurrence and the likely benefits of chemotherapy treatment. The majority of cases of ER-positive breast cancer fall in between these two extremes, and decisions regarding the addition of chemotherapy to adjuvant endocrine therapy should be individualized based on patient and disease factors. Gene expression profiles performed in women with ER-positive, HER2-negative disease are useful when the decision regarding whether or not to use chemotherapy is unclear.

When to use a gene expression profile
Gene expression Oncotype DX Recurrence Score (RS) and EndoPredict have been developed to identify patients with such a low chance of recurrence that the absolute benefit of chemotherapy may not justify the risk of toxicities. For the RS, prospective, randomized clinical trials do not demonstrate that women with low scores (less than 26) benefit from the addition of chemotherapy. By contrast, patients with higher scores on these assays have a sufficiently high risk of recurrence despite endocrine therapy that the addition of chemotherapy outweighs the risk of toxicities.

These assay should not be used in women who are not candidates for chemotherapy since the results would not alter management. This might include patients with absolute contraindications to chemotherapy due to baseline health concerns or frailty, or women who for other reasons will not consider chemotherapy.
Gene expression profiling for the management of breast cancer is medically necessary when **ALL** of the following criteria are met:

1. The tumor is either ER-positive or progesterone receptor (PR)-positive, or both are positive; **AND**
2. The tumor is HER2 negative; **AND**
3. **ONE** of the following:
   a. Tumor is $\geq 0.6$ cm to $< 1$ cm in diameter with moderate/poor differentiation; **OR**
   b. Tumor $> 1$ cm in diameter; **AND**
4. **ONE** of the following:
   a. Axillary lymph nodes are negative (pNO); **OR**
   b. Axillary lymph nodes contain $\leq 2$ mm micrometastases (PN1 mi); **AND**
5. Patient is a candidate for adjuvant chemotherapy.

**Not Medically Necessary:**
Gene expression profiling for the management of breast cancer is not medically necessary in any of the following situations:

1. Repeat testing for the same tumor.
2. Patients with bilateral breast tumors.
3. The patient is NOT a candidate for adjuvant chemotherapy.
4. There is involvement of 1-3 ipsilateral axillary lymph nodes (low evidence).
5. When the initial surgery and biopsy were performed more than 6 months prior to ordering gene expression profiling.
6. When there are multiple ipsilateral tumors, multiple tests for each tumor type are not medically necessary. Only the tumor with the most aggressive histologic characteristics should be tested.
7. Testing should not be performed on a preliminary biopsy. Testing should be requested only when the tumor has been surgically removed and a pathology examination and report have been completed.

**Coding**

81519  Oncology (breast), mRNA, gene expression profiling by real-time RT-PCR of 21 genes, utilizing formalin-fixed paraffin embedded tissue, algorithm reported as recurrence score.

81522  Oncology (breast), mRNA, gene expression profiling by RT-PCR of 12 genes (8 content and 4 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as recurrence risk score.

**References**

EncoderPro Optum 360.

Foukakis T, Bergh J, Hurvitz S. Deciding when to use adjuvant chemotherapy for hormone receptor-positive, HER2-negative breast cancer. UpToDate, topic last updated: Apr 15, 2020.


Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

Criteria Change History

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<td>Title changed, added narrative, revised criteria, references updated.</td>
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