FEP 2.03.01 In Vitro Chemoresistance and Chemosensitivity Assays

Description
In vitro chemoresistance and chemosensitivity assays have been developed to provide information about the characteristics of an individual patient’s malignancy to predict potential responsiveness of their cancer to specific drugs. These assays are sometimes used by oncologists to select treatment regimens for a patient. Several assays have been developed that differ concerning the processing of biologic samples and detection methods. However, all involve similar principles and share protocol components including (1) isolation of cells and establishment in an in vitro medium (sometimes in soft agar); (2) incubation of the cells with various drugs; (3) assessment of cell survival; and (4) interpretation of the result.

FDA 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. Chemoresistance and chemosensitivity assays discussed in this review are available under the auspices of the Clinical Laboratory Improvement Amendments. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.

POLICY STATEMENT
In vitro chemoresistance assays, including, but not limited to, Extreme Drug Resistance assay, are considered investigational.

In vitro chemosensitivity assays, including, but not limited to, the Histoculture Drug Response Assay, a fluorescent cytoprint assay, the ChemoFX assay, or the CorrectChemo assay, are considered investigational.

BENEFIT APPLICATION
Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

Chemotherapy resistance and sensitivity assays are specialized laboratory tests typically performed in reference laboratories.

Effective Date: January 15, 2018
Related Policies: None
RATIONALE

Summary of Evidence
For individuals who have cancer who are initiating chemotherapy who receive chemoresistance assays, the evidence includes correlational observational studies. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, and quality of life. Some retrospective and prospective correlational studies have suggested that chemoresistance assays may be associated with chemotherapy response. However, prospective studies have not consistently demonstrated that chemoresistance assay results are associated with survival. Furthermore, no studies were identified that compared outcomes for patients managed using assay-directed therapy with those managed using physician-directed therapy. Large, randomized, prospective clinical studies comparing overall survival are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have cancer who are initiating chemotherapy who receive chemosensitivity assays, the evidence includes a randomized controlled trial, nonrandomized studies, and correlational observational studies. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, and quality of life. The most direct evidence on the effectiveness of chemosensitivity assays in the management of patients with cancer comes from several studies comparing outcomes for patients managed using a chemosensitivity assay with those managed using standard care, including a randomized controlled trial. Although some improvements in tumor response were noted in the randomized controlled trial, there were no differences in survival outcomes. One small nonrandomized study reported improved overall survival in patients receiving chemosensitivity-guided therapy compared with patients receiving standard chemotherapy. A number of retrospective and prospective studies of several different chemosensitivity assays have suggested that patients whose tumors have higher chemosensitivity have better outcomes. Currently, additional studies to determine whether the clinical use of in vitro chemosensitivity testing leads to improvements in overall survival are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

National Comprehensive Cancer Network
Current National Comprehensive Cancer Network (NCCN) guidelines for the treatment of epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer (v.2.2017) state that “Chemosensitivity/resistance and/or other biomarker assays are being used in some NCCN Member Institutions. The current level of evidence is not sufficient to supplant standard-of-care chemotherapy. (category 3).”

NCCN guidelines for the treatment of gastric cancer (v.2.2017) and uterine neoplasms (v.3.2017) do not discuss the use of chemoresistance or chemosensitivity assays as part of cancer management.

American Society of Clinical Oncology
The updated 2011 American Society of Clinical Oncology clinical guidelines on the use of chemotherapy sensitivity and resistance assays did not recommend use of chemotherapy sensitivity and resistance assays unless in a clinical trial setting.

U.S. Preventive Services Task Force Recommendations
Not applicable.
Medicare National Coverage

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

REFERENCES

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POLICY HISTORY

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Description</th>
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<tbody>
<tr>
<td>December 2011</td>
<td>New Policy</td>
<td>Policy statement changed to not medically necessary.</td>
</tr>
<tr>
<td>June 2012</td>
<td>Update Policy</td>
<td>Policy updated with literature review. References 2, 3, 21, and 40 added, some reordered. No change to policy statement.</td>
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<tr>
<td>June 2013</td>
<td>Update Policy</td>
<td>Policy updated with literature review. References 6-8, 40-42, 45, and 47-48 added. Background and rationale reorganized. No changes to policy statements.</td>
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<tr>
<td>June 2015</td>
<td>Update Policy</td>
<td>Policy updated with literature review. References 4, 41-42, and 50 added. “ChemoFx” and “CorrectChemo” added to the list on investigational chemosensitivity assays; policy statements otherwise unchanged.</td>
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<tr>
<td>December 2016</td>
<td>Update Policy</td>
<td>Policy updated with literature search; reference 42 added. Policy statements unchanged.</td>
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</table>
| December 2017   | Update Policy| Policy updated with literature search through June 20, 2017; reference 35 and 49 added. Policy statements corrected from "not

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