



FEP Medical Policy Manual

FEP 2.03.01 In Vitro Chemoresistance and Chemosensitivity Assays

Effective Policy Date: October 1, 2020

Related Policies:

Original Policy Date: December 2011

None

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. Oncologists may sometimes use these assays 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.

OBJECTIVE

The objective of this evidence review is to determine whether the use of chemoresistance and chemosensitivity assays improve the net health outcome in individuals being treated for cancer.

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, or the ChemoFX assay, are considered **investigational**.

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POLICY GUIDELINES

None

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.

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.

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 (OS), 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 OS 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 OS, 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 trial, there were no differences in survival outcomes. One small nonrandomized study reported improved OS 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 OS are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

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SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

National Comprehensive Cancer Network

Epithelial Ovarian Cancer/ Fallopian Tube Cancer/ Primary Peritoneal Cancer

Current NCCN (v.1.2020) guidelines for the treatment of epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer state that "Chemosensitivity/resistance and/or other biomarker assays are being used in some NCCN Member Institutions for decisions related to future chemotherapy in situations where there are multiple equivalent chemotherapy options available. The current level of evidence is not sufficient to supplant standard-of-care chemotherapy (category 3)."[54](#).

Gastric Cancer

The NCCN (v.2.2020) guidelines for the treatment of gastric cancer do not discuss the use of chemoresistance or chemosensitivity assays as part of cancer management.[55](#).

Breast Cancer

The NCCN (v.4.2020) guidelines for the treatment of breast cancer do not discuss the use of chemoresistance or chemosensitivity assays as part of cancer management.[56](#).

Melanoma

The NCCN (v.3.2020) guidelines for the treatment of cutaneous melanoma do not discuss the use of chemoresistance or chemosensitivity assays as part of cancer management.[57](#).

Non-Small Cell Lung Cancer

The NCCN (v.6.2020) guidelines for the treatment of non-small cell lung cancer do not discuss the use of chemoresistance or chemosensitivity assays as part of cancer management.[58](#).

Uterine Neoplasms

The NCCN (v.1.2020) guidelines for the treatment of uterine neoplasms do not discuss the use of chemoresistance or chemosensitivity assays as part of cancer management.[59](#).

American Society of Clinical Oncology

The updated American Society of Clinical Oncology (2011) clinical guidelines on the use of chemotherapy sensitivity and resistance assays did not recommend the use of chemotherapy sensitivity and resistance assays unless in a clinical trial setting.[60](#).

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U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

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

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POLICY HISTORY - THIS POLICY WAS APPROVED BY THE FEP® PHARMACY AND MEDICAL POLICY COMMITTEE ACCORDING TO THE HISTORY BELOW:

Date	Action	Description
December 2011	New policy	
June 2012	Replace policy	Policy statement changed to not medically necessary
June 2013	Replace policy	Policy updated with literature review. References 2, 3, 21, and 40 added, some reordered. No change to policy statement.
June 2014	Replace policy	Policy updated with literature review. References 6-8, 40-42, 45, and 47- 48 added. Background and rationale reorganized. No changes to policy statements.

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Date	Action	Description
June 2015	Replace policy	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.
December 2016	Replace policy	Policy updated with literature search; reference 42 added. Policy statements unchanged.
December 2017	Replace policy	Policy updated with literature search through June 20, 2017; reference 35 and 49 added. Policy statements corrected from "not medically necessary to investigational."
September 2018	Replace policy	Policy updated with literature search through May 7, 2018; reference 9 added. CorrectChemo assay removed from the second policy statement; intent of statements unchanged.
September 2019	Replace policy	Policy updated with literature search through May 13, 2019; no references added. Policy statements unchanged.
September 2020	Replace policy	Policy updated with literature review through April 24, 2020; no references added. Policy statements unchanged.

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