

## IN VITRO CHEMORESPONSE ASSAYS

**Policy number:** 200805-0001

**Effective date:** 05/27/2008

**Revision date:** N/A

### Overview

In vitro, also referred to as ex vivo, chemoresponse (chemotherapy sensitivity and chemotherapy resistance) assays have been proposed as a means of predicting tumor response to various chemotherapy agents. Chemoresponse assays are intended to assist with the selection of chemotherapy agents for the treatment of cancer in individual patients.

Assay-guided therapy has been proposed as an alternative to empiric therapy. In assay-guided therapy, tumor cells from the individual patient are exposed to chemotherapeutic agents in vitro. Empiric therapy refers to the selection of chemotherapy agents based on the critical evaluation of outcome evidence from well-designed clinical trials.

The enthusiasm for chemotherapy sensitivity (chemosensitivity) assays has diminished over the years due to poor positive predictive values (i.e., the likelihood that agents shown to be effective in vitro will produce a similar clinical response), suggesting that factors other than the inherent chemosensitivity of tumor cells significantly influence the outcome of chemotherapy in vivo.

The negative predictive value of chemotherapy resistance (chemoresistance) assays is very high (>99%), such that the possibility of inappropriately deselecting effective chemotherapy is remote. However, improved survival among patients in whom the results of chemoresistance assays were used to choose chemotherapy regimens over empiric therapy has not been demonstrated. Advocates of chemoresistance assays argue that the avoidance of unnecessary toxicity is the relevant outcome, and that the outcome of improved survival, which is appropriate for chemosensitivity assays, is not relevant for chemoresistance assays. However, when one or more agents are eliminated on the basis of chemoresistance assays, it is implied that the remaining agents are effective. It has not been shown that agents that do not show chemoresistance are more effective, therefore, the selection of optimal chemotherapy becomes a combination of the two processes (chemoresistance and chemosensitivity), and survival is the relevant outcome.

In 2004, the American Society of Clinical Oncology (ASCO) established a Working Group to develop a technology assessment for chemotherapy sensitivity and resistance assays in order to define the role of these tests in routine oncology practice. The Working Group collaborated with the Blue Cross and Blue Shield Association (BCBSA) Technology Evaluation Center. The ASCO Working Group made the following recommendation: *"The use of chemotherapy sensitivity and resistance assays to select chemotherapeutic agents for individual patients is not recommended outside of the clinical trial setting. Oncologists should make chemotherapy treatment recommendations on the basis of published reports of clinical trials and a patient's*

*health status and treatment preferences. Because the in vitro analytic strategy has potential importance, participation in clinical trials evaluating these technologies remains a priority.*" (Schrag et al.)

Lab tests are medically necessary when they provide clinically useful information that leads to improved patient outcomes. A May 2008 review of peer-reviewed published literature did not reveal any prospective randomized controlled studies providing strong evidence of improved patient survival using assay-guided therapy over empiric therapy. Well-designed clinical trials are needed to determine the future clinical role of assay-guided therapy.

## Definitions

**In vitro:** that which takes place within a glass, Petri dish or test tube.

**Ex vivo:** that which takes place outside an organism; ex vivo refers to experimentation done in or on living tissue in an artificial environment outside the organism.

**Chemosensitivity assays:** chemosensitivity refers to the ability of an agent to kill target cells; hence chemosensitivity assays are used to "select" potential chemotherapy agents, i.e., chemosensitivity assays are used to potentially determine the specific chemotherapeutic agent(s) to which a patient's tumor would respond.

**Chemoresistance assays:** chemoresistance refers to the ability of target cells to withstand exposure to an agent; hence chemoresistance assays are used to "deselect" potential chemotherapy agents, i.e., chemoresistance assays are used to potentially determine the specific chemotherapeutic agent(s) to which a patient's tumor would not respond.

## Covered Services

In vitro chemoresponse assays are not covered. FCHP considers in vitro chemoresponse assays, such as ChemoFx® (Precision Therapeutics, Inc.) or Oncotech EDR® (Oncotech, Inc.) experimental/investigational.

## Codes

There is no specific CPT or HCPCS code for in vitro chemoresponse assays. The most appropriate CPT code is 89240 (Unlisted miscellaneous pathology test).

Codes	Number	Description
CPT	89240	Unlisted miscellaneous pathology test

## References

1. Samson DJ, Seidenfeld J, Ziegler K, Aronson N. Chemotherapy sensitivity and resistance assays: a systematic review. *J Clin Oncol.* 2004 Sep 1;22(17):3618-30. Epub 2004 Aug 2.
2. Deborah Schrag, Harinder S. Garewal, Harold J. Burstein, David J. Samson, Daniel D. Von Hoff, and Mark R. Somerfield. American Society of Clinical Oncology Technology Assessment: Chemotherapy Sensitivity and Resistance Assays. *J Clin Oncol.* 2004;22(17):3631-3638.

3. Ugurel S, Schadendorf D, Pföhler C, Neuber K, Thoelke A, Ulrich J, Hauschild A, Spieth K, Kaatz M, Rittgen W, Delorme S, Tilgen W, and Reinhold U. In vitro drug sensitivity predicts response and survival after individualized sensitivity-directed chemotherapy in metastatic melanoma: a multicenter phase II trial of the Dermatologic Cooperative Oncology Group. *Clin Cancer Res.* 2006 Sep 15;12(18):5454-63.
4. Iwahashi M, Nakamori M, Nakamura M, Noguchi K, Ueda K, Nakatani Y, Ojima T, Ishida K, Naka T, Yamaue H. Individualized adjuvant chemotherapy guided by chemosensitivity test sequential to extended surgery for advanced gastric cancer. *Anticancer Res.* 2005 Sep-Oct;25(5):3453-9.
5. Tavassoli FA, Cook CB, Pestaner JP. A comparison of two commercially available in vitro chemosensitivity assays. *Oncology.* 1995 Sep-Oct;52(5):413-8.
6. Wu B, Zhu JS, Zhang Y, Shen WM, Zhang Q. Predictive value of MTT assay as an in vitro chemosensitivity testing for gastric cancer: One institution's experience. *World J Gastroenterol.* 2008 May 21;14(19):3064-8.
7. Xiao Y, Li JD, Shi HL, Liu JH, Feng YL, Li MD. Predictive value of in vitro MTT assay chemosensitivity test of cytotoxic drug activity in cervical cancer. *Ai Zheng.* 2007 Apr;26(4):386-9.
8. Kubota T, Weisenthal L. Chemotherapy sensitivity and resistance testing: to be "standard" or to be individualized, that is the question. *Gastric Cancer.* 2006;9(2):82-7.
9. Taylor CG, Sargent JM, Elgie AW, Williamson CJ, Lewandowicz GM, Chappatte O, Hill JG. Chemosensitivity testing predicts survival in ovarian cancer. *Eur J Gynaecol Oncol.* 2001;22(4):278-82.

### Products to Which This Policy Applies

- ⊕ FCHP Direct & Select Care
- ⊕ Fallon Preferred Care (PPO)
- ⊕ Major Medical
- ⊕ MassHealth
- ⊕ Companion Care
- ⊕ Commonwealth Care
- ⊕ Fallon Senior Plan™

### Committee review dates:

Technology Assessment Subcommittee: 05/27/2008, 06/24/2008

Technology Assessment Committee: 10/14/2008

#### IMPORTANT NOTE

**Not all services are covered for all products or employer groups.** This medical policy expresses FCHP's determination of whether certain services or supplies are medically necessary, experimental or investigational or cosmetic. FCHP has reached these conclusions based upon the regulatory status of the technology and a review of clinical studies published in peer-reviewed medical literature. Even though this policy may indicate that a particular service or supply is considered covered, this conclusion is not based upon the terms of your particular benefit plan. Each benefit plan contains its own specific provisions for coverage and exclusions. Not all benefits that are determined to be medically necessary will be covered benefits under the terms of your benefit plan. Members and their providers need to consult the Evidence of Coverage to determine if there are any exclusions or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and the plan of benefits, the provisions of the benefits plan will govern. However, applicable state mandates will take precedence with respect to fully insured plans and self-funded non-ERISA (e.g., government, school boards, church) plans. Unless otherwise specifically excluded, Federal mandates will apply to all plans. With respect to Medicare and Medicaid members, this policy will apply unless Medicare and Medicaid policies extend coverage beyond this medical policy.