



March 1, 2010

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J1 Part B Medical Affairs
P.O. Box 1476
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Reference: LCD ID # DL30697, In Vitro Chemosensitivity & Chemoresistance Assays

Dear Ms. Collins:

On behalf of the members of the American Clinical Laboratory Association (ACLA), I am submitting comments on the draft local coverage determination denying coverage for chemosensitivity and chemoresistance assays (CSRAs) because of insufficient published evidence-based data (clinical utility) to justify coverage.

The level of evidence required to justify coverage of diagnostic testing can vary depending on the applications of the particular diagnostic test. Where a test is being used to confirm a diagnosis, less rigorous may be sufficient to demonstrate the utility of the test. Where significant therapeutic decisions may be made based on the test results, a higher level of evidence may be required. However, there are already well accepted standards for judging most clinical, diagnostic testing, standards which focus on two necessary and complementary requirements. First, does the test consistently and accurately measure the analyte for which it is testing? Second, does it consistently identify the clinical condition associated with the analyte in the patient population for whom the test is intended? Beyond analytical and clinical validity, an assessment of the utility of a diagnostic test should be informed evidence of the extent to which the results of the test can influence patient management. The perceived benefits gained from lengthy, comprehensive evidentiary methodologies must be balanced against the significant opportunity costs such methodologies often can impose, including disincentives to medical innovation and delayed or denied access to diagnostics that could have avoided or mitigated negative health outcomes and their associated costs.

There is a broad spectrum of evidence that can and should be considered in evaluating diagnostic tests. While randomized clinical trials (RCTs) may be the “gold” standard for some procedures and therapies, they have significant limitations when applied to many diagnostic situations. The difficulties of constructing RCTs are complicated by rapid changes in therapeutic approaches where the drug regimens used to treat patients are in constant states of revisions. Scientifically sound alternative approaches must be considered.

CSRAs are a case in point. They assist physicians with the selection of chemotherapy drugs at initial diagnosis or at tumor recurrence. They can determine whether a tumor growth is inhibited by a known chemotherapy drug or drug combination. They are not intended to replace physician judgment as a standard of care to determine treatment for every patient across all tumor types but to provide additional information integrated with physician judgment for those patients with difficult to treat cancer types where multiple or no standard of care exist. In effect, they complement the physician’s experience and can provide valuable patient-specific information, particularly when there is non-uniform response to standard regimens or no clear choice for the next regimen. There is a large body of evidence, much of which is positive. In addition to this, the NCCN 2010 Ovarian, Fallopian, and Peritoneal Cancer Guidelines recently added the following language regarding the use of Chemosensitivity/resistance assays by some NCCN centers reflecting the intended use of the tests:

“Chemosensitivity/resistance assays are being used in some NCCN centers 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 therapy (category 3).”

CSRAs can be of invaluable assistance to physicians in determining the course of treatment of their patients. Each CSRA should be considered for individual coverage determination based on a review of the assay specific data rather than a determination that there is insufficient evidence to justify coverage of any CSRA assay.

We thank you for the opportunity to submit these comments.

Sincerely,

A handwritten signature in black ink, appearing to read 'JoAnne Glisson', with a stylized flourish at the end.

JoAnne Glisson
Senior Vice President