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Date of request: June 20, 2014  
NCCN Guidelines™ Panel: Breast Cancer

On behalf of Janssen Diagnostics LLC, I respectfully request the NCCN Guidelines™- Breast Cancer Panel to review the enclosed data for inclusion of the CELLSEARCH® Circulating Tumor Cell Test as an aid in monitoring disease progression for metastatic breast cancer patients.

**Specific Change:**

Recommend the CELLSEARCH® Circulating Tumor Cell Test as a component of the diagnostic evaluation of patients with metastatic breast cancer at baseline prior to initiating a new cycle of chemotherapy and at 3 weeks post initiation of therapy with a category 1 evidence level rating.

**FDA Clearance:**

The CELLSEARCH® CTC test is FDA-cleared for the monitoring of patients with metastatic breast, colorectal and prostate cancer.<sup>1</sup>

**Rationale:**

In a Phase 3, prospective, randomized clinical study, (SWOG S0500), CELLSEARCH® CTC enumeration demonstrated that the median OS for patients with  $\geq 5$  CTCs, whose CTC levels decreased to  $< 5$  after 1 cycle of therapy was 23 months, reflecting therapy response. For patients whose CTC levels continued to be  $\geq 5$  OS was only 13 months, reflecting resistance to the administered therapy.

Patients falling into a poor prognosis category (defined by CTC  $\geq 5$  cells at baseline and after 1 cycle of therapy) showed no difference in OS (10.7 and 12.5 months) or PFS (3.5 months and 4.6 months) whether they were treated according to current clinical standards or switched immediately to a new therapy.

The study concluded that CTC results are actionable. Failure to reduce CTC within the first 3-4 weeks of starting first-line chemotherapy in patients with mBC portends poor prognosis and is indicative of general chemoresistance. Patients who are found to have more than five CTCs after one cycle of chemotherapy should strongly consider participating in trials of novel therapeutic agents at the time of progression, rather than moving on to second or later lines of chemotherapy.<sup>2</sup>

These results are confirmed by findings from a pooled analysis of 1944 patients, with metastatic breast cancer, recently published in Lancet Oncology. During the first weeks of chemotherapy, CTC count is shown to be a significant early predictor of survival, demonstrating the clinical value of CTC testing prior to or after initiating chemotherapy.<sup>3</sup>

Additionally, it is significant to note that on February 19, 2013 the official German Breast Cancer Group (Arbeitsgemeinschaft Gynäkologische Onkologie, AGO) issued a recommendation supporting CTCs measured by CELLSEARCH® technology as an important factor in decision making for patients with mBC.<sup>4</sup>

The following publications are submitted with the Full Package Insert. We would like to acknowledge the contributions of the NCCN panel members who are also co-authors of some of these publications.

1. CellSearch™ Circulating Tumor Kit, INSTRUCTIONS FOR USE, Distributed by Janssen Diagnostics, LLC. Raritan, NJ. June 2014.
2. Smerage, J. B., et al. (2014). Circulating Tumor Cells and Response to Chemotherapy in Metastatic Breast Cancer. J Clin Oncol, published ahead of print, June 2014.
3. Bidard, F. C., et al. (2014). Clinical validity of circulating tumour cells in patients with metastatic breast cancer: a pooled analysis of individual patient data. Lancet Oncol 15, 406-14.
4. Arbeitsgemeinschaft Gynäkologische Onkologie, 2013. (English translation from Janssen Diagnostics, LLC)

Sincerely,

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