PACIFIC EDGE DIAGNOSTICS USA LTD

To: submission@nccn.org
Re: Submission Request – Bladder Cancer

Submitted by:
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Date of Request: August 13, 2020
NCCN Guidelines Panel: Bladder Cancer – September 2020

On behalf of Pacific Edge Diagnostics, I respectfully request the ***NCCN Bladder Cancer Guideline Panel*** to review the enclosed data[1-8] that supports expanded use of urinary urothelial tumor markers for evaluation of patients with a history of bladder cancer who are under surveillance.

Specific Changes:

- On **BL-E** page 1, **Table 2: Low-Risk, Non-Muscle-Invasive Bladder Cancer, Urine tests** add the bullet point "Consider urinary urothelial tumor markers".
- On **BL-E** page 2, **Table 3: Intermediate Risk, Non-Muscle-Invasive Bladder Cancer, Urine tests**, add the bullet point "Consider urinary urothelial tumor markers".

FDA Clearance: FDA clearance is not required for Cxbladder because the assay is performed in the central laboratory at Pacific Edge Diagnostics USA. This laboratory is regulated and certified under the Clinical Laboratory Improvement Amendments (CLIA) and the College of American Pathologists (CAP).

Rationale to extend use: The current NCCN guidelines include "Consider urinary urothelial tumor markers" on **BL-E** page 2, **Table 4: High-Risk, Non-Muscle-Invasive Bladder Cancer for years 1 and 2**. The value of these biomarker tests in high-risk patients was traditionally to enhance the detection of recurrent disease. More recent literature shows that urinary urothelial tumor markers with high sensitivity and NPV can be safely used in low, intermediate and high-risk patients to manage the intervals for cystoscopy in select patients[1,2,3]. As noted on **MS-13** for high-risk patients, cystoscopy should be performed within a range of 3-6 months, giving flexibility for managing individual patients. Data by Koya[3] and Gagnon[4] suggests that low-intensity monitoring may be safe in high-risk patients. Urothelial tumor biomarker tests that have high sensitivity and NPV can customise the cystoscopy interval within the recommended ranges by ruling out disease in select patients. Cxbladder Monitor has been shown to have sufficient sensitivity and NPV to enhance patient-physician shared decision making and allow clinicians and patients to safely personalize surveillance evaluations[3,5,6,7]. Cxbladder Monitor can be performed on urine that is self-sampled by patients at home, providing addional advantages to patients at risk from COVID-19 infection and helping to manage both in-person and by telemedicine surveillance during the ongoing pandemic. Recent publication of the adoption of urinary biomarkers to support teleconsultations by Kaiser Permanente[8], provide further support for this recommendation to expand the use of biomarker tests in bladder cancer surveillance.

We recommend that the use of urinary biomarkers is expanded and changed to Category 2A so that patients with bladder cancer also gain full access to advanced, high performance, genomic tests.

Please note that the current recommendation for use of urinary urothelial tumor markers is designated as Category 2B. This designation may actually be used by some insurers as a reason to deny coverage of tests, thereby limiting access to precision diagnostics. Biomarker assays are improving patient care across multiple disease areas but patients with bladder cancer have been underserved in their access to precision diagnostics.

The following peer reviewed, published, journal articles (1-7), along with an Op-Ed from Dr. Gin of Kaiser Permanente (8), are submitted in support of the recommended changes to the NCCN guidelines 2020:

1. Lozano F et al. Current status of genetic urinary biomarkers for surveillance of non-muscle invasive bladder cancer: a systemic review. BMC Urology 2020
2. Bhat A et al. Urinary biomarkers in bladder cancer: where do we stand? *Current Opinion in Urology* 2019;29(3):203-209.
3. Koya M et al. An evaluation of the real-world use and clinical utility of the Cxbladder Monitor assay in the follow-up of patients previously treated for bladder cancer. *BMC Urology.* 2020;20(12).
4. Gagnon L. Is low-intensity surveillance feasible for patients with high-risk NMIBC? *Urology Times* 2020; 48(07):29-30.
5. Kavalieris L et al. Performance characteristics of a multigene urine biomarker test for monitoring for recurrent urothelial carcinoma in a multicenter study. *J Urol.* 2017;197(6):1419-26.
6. Lotan Y et al. Clinical comparison of non-invasive urine tests for ruling out recurrent urothelial carcinoma. *Urol Oncol.* 2017; Mar 30.
7. Konety et al. Evaluation of Cxbladder and Adjudication of Atypical Cytology and Equivocal Cystoscopy. *European Urology* 2019
8. Gin, N. Improvements in Care Delivery-Pandemic brings much-needed transformational jolt. MedPage Today 2020; Jul 26

Sincerely,

T. Nifong M.D.

Thomas P. Nifong, MD, Medical Director