Medical Coverage Policy | Urinary Tumor Markers for Bladder Cancer

EFFECTIVE DATE: | |
POLICY LAST UPDATED: 07|02|2015

OVERVIEW
This policy documents the coverage determination for Urinary Tumor Markers for Bladder Cancer. The diagnosis of bladder cancer is generally made by cystoscopy and biopsy. Moreover, bladder cancer has a very high frequency of recurrence and therefore follow-up cystoscopy, along with urine cytology, is done periodically to identify recurrence early. Urine biomarkers that might be used to either supplement or supplant these tests have been actively investigated.

MEDICAL CRITERIA
Not applicable

PRIOR AUTHORIZATION
Not applicable

POLICY STATEMENT
BlueCHiP for Medicare and Commercial Products

The use of urinary tumor markers is considered not medically necessary in the diagnosis of, monitoring, and/or screening for bladder cancer as there is insufficient peer-reviewed literature that demonstrates that the service is effective.

COVERAGE
Benefits may vary between groups/contracts. Please refer to the appropriate Evidence of Coverage or Subscriber Agreement for limitations of benefits/coverage when services are not medically necessary.

BACKGROUND
Urinary bladder cancer, a relatively common form of cancer in the United States, results in significant morbidity and mortality. Bladder cancer (urothelial carcinoma), typically presents as a tumor confined to the superficial mucosa of the bladder. The most frequent symptom of early bladder cancer is hematuria; however, UT symptoms (ie, urinary frequency, urgency, dysuria) may also occur.

For patients with hematuria, American Urological Association guidelines recommend cystoscopic evaluation of all adults older than age 40 years with microscopic hematuria and for those younger than age 40 years with risk factors for developing bladder cancer. Confirmatory diagnosis of bladder cancer is made by cystoscopic examination, considered to be the criterion standard, and biopsy. At initial diagnosis, approximately 70% of patients have cancers confined to the epithelium or subepithelial connective tissue. Nonmuscle invasive disease is usually treated with transurethral resection, with or without intravesical therapy, depending on depth of invasion and tumor grade. However, a 50% to 75% incidence of recurrence has been noted in these patients, with 10% to 15% progressing to muscle invasion over a 5-year period. Current follow-up protocols include flexible cystoscopy and urine cytology every 3 months for 1 to 3 years, every 6 months for an additional 2 to 3 years, and then annually thereafter, assuming no recurrence.

While urine cytology is a specific test (from 90%-100%), its sensitivity is lower, ranging from 50% to 60% overall and is considered even lower for low-grade tumors. Therefore, interest has been reported in identifying tumor markers in voided urine that would provide a more sensitive and objective test for tumor recurrence.

Tests cleared by FDA include the following. The BTA stat® test (Polymedco, Cortlandt Manor, NY) is a qualitative, point-of-care test with an immediate result that identifies a human complement factor H-related protein that was shown to be produced by several human bladder cell lines but not by other epithelial cell lines. The BTA stat® test is an in vitro immunoassay intended for the qualitative detection of bladder tumor-associated antigen in the urine of persons diagnosed with bladder cancer.

The BTA TRAK® test (Polymedco, Cortlandt Manor, NY) provides a quantitative determination of the same protein. This test requires trained personnel and a reference laboratory. Both tests have sensitivities comparable with that of cytology for high-grade tumors and better than cytology for low-grade tumors. Nuclear matrix protein 22 (NMP22) is a protein associated with the nuclear mitotic apparatus. It is thought that this protein is released from the nuclei of tumor cells during apoptosis. Normally, only very low levels of NMP22 can be detected in the urine, and elevated levels may be associated with bladder cancer. NMP22 may be detected in the urine using an immunoassay.

Fluorescence in situ hybridization (FISH) DNA probe technology has also been used to detect chromosomal abnormalities in voided urine to assist not only in bladder cancer surveillance but also in the initial identification of bladder cancer. FISH DNA probe technology is a technique to visualize nucleic acid sequences within cells by creating short sequences of fluorescently labeled, single-strand DNA, called probes, which match target sequences. The probes bind to complementary strands of DNA, allowing for identification of the location of the chromosomes targeted. Vysis UroVysion® (Abbott Molecular) is a commercially available FISH test.

The ImmunoCyt™ test (DiagnoCure Inc., Quebec City, QC) uses fluorescence immunohistochemistry with antibodies to a mucin glycoprotein and a carcinoembryonic antigen. These antigens are found on bladder tumor cells. The test is used for monitoring bladder cancer in conjunction with cytology and cystoscopy.

In addition to the FDA-cleared tests, clinical laboratories that meet Clinical Laboratory Improvement Act standards are marketing urine-based tests. For example, Predictive Laboratories (Lexington, MA) markets a test called CertNDx™, to assess fibroblast growth factor receptor 3 (FGFR3) mutations. The test is intended to be used in combination with cytology for identifying patients with hematuria at risk of bladder cancer. FGFR3 mutations may be associated with lower grade bladder tumors that have a good prognosis. In addition, Pacific Edge (New Zealand) is marketing a test in the United States called Cxbladder™, which tests for 5 urine-based markers.

Numerous studies have evaluated the accuracy of the urinary tumor markers bladder tumor antigen (BTA) stat, nuclear matrix protein 22 (NMP22), UroVysion, and ImmunoCyt for diagnosing and/or monitoring bladder cancer. These urinary tumor markers tend to have higher sensitivity but not higher specificity than cytology, and combining tumor markers with cytology can improve overall diagnostic accuracy. There is insufficient evidence that urinary tumor markers improve the accuracy of initial diagnosis of UUT disease or monitoring patients with a history of UT disease for upper tract recurrence. There is little evidence on the impact of urinary bladder tumor marker tests on patient management, eg, frequency of cystoscopy, or the impact of tests on health outcomes. Moreover, there is also a lack of evidence on the impact of screening asymptomatic subjects for bladder cancer using urinary tumor markers. In 2012 to 2013, the evidence on the use of urinary tumor markers was re-evaluated with focus on whether clinical utility had been established. It was concluded that, due to continued lack of published evidence of clinical utility, mixed input from clinical input on whether results of urinary tumor marker tests lead to change in patient management, and a lack of support for urinary marker use from clinical practice guidelines, the use of urinary tumor markers is considered not medically necessary.

CODING

BlueCHiP for Medicare and Commercial Products

The following services are considered not medically necessary:

86294 86316 86386
88120 88121

RELATED POLICIES

Immunoassay for Tumor Antigens

PUBLISHED

Provider Update, 2015

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