JM Palmetto - Lab: Bladder/Urothelial Tumor Markers

CPT: 86294, 86316, 86386, 88120, 88121

CMS Policy for Alabama, Georgia, North Carolina, South Carolina, Tennessee, Virginia, and West Virginia

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Medically Supportive ICD Codes are listed on subsequent page(s) of this document.

INDICATIONS

Gross painless hematuria is often the first manifestation of an urothelial tumor. Since the degree of hematuria bears no relation to the seriousness of the underlying disease, the microscopic finding of blood in the urine is a serious symptom until significant pathology has been excluded.

At this time, there is no published consensus from the following national organizations: National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO), American Urological Association (AUA) and the International Bladder Cancer Consensus Group (IBCCG) regarding the management of persistent asymptomatic microscopic hematuria. Due to insufficient supporting data, the AUA's 2001 best practices policy could not recommend routine use of voided urinary markers in the evaluation of patients with microscopic hematuria[3].

Recommended surveillance schedules for patients with a previous negative evaluation for unexplained microscopic hematuria include annual urinalysis and voided urinary cytology until the hematuria resolves, or for up to three years if microscopic hematuria persists. The AUA has been silent regarding practice guidelines due to the paucity of prevalence studies on asymptomatic microscopic hematuria.

Cystoscopy in conjunction with bladder tumor markers is the standard practice to evaluate patients with symptoms suggesting bladder cancer and to monitor treated patients for recurrence or progression. Although cystoscopy is considered the "gold standard", studies have shown that up to 20% of tumor can be missed. Urinary cytology has close to a 90%-100% specificity, but only 10%-50% sensitivity for low grade urinary cancer (UC) detection. Due to this deficit, clinicians have sought noninvasive tumor markers detectable in urine.

Upwards of 50% of patients have recurrence of bladder cancer within five (5) years.

After initial diagnosis and treatment, patients with UC are frequently monitored every three months for the first two years, every four months for the third year then usually twice a year for the fourth year. Annual monitoring is recommended during years 5 through 15.

Diagnostic and Surveillance Tests

- **BTA TRAK®** - a quantitative determination of human complement factor H-related protein
- **Nuclear matrix protein 22 (NMP-22)** – detects nuclear mitotic apparatus protein believed to be released during apoptosis; a quantitative assay, which is either positive of negative
- **NMP-22 BladderChek®** – a CLIA-waved assay, point of care test with an immunochromographic qualitative format taking 20 minutes to perform
- **The UroVysion®** Bladder Cancer Kit is fluorescence in situ hybridization (FISH) DNA probe technology. It is designed to detect aneuploidy for chromosomes 3, 7, 17 and loss of the 9p21 locus. This assay involves visualization of nucleic acid sequences within cells by creating short sequences of fluorescently labeled, single-strand DNA probes that match target sequences. The probes bind to complementary strands of DNA to identify the targeted chromosome(s) location. It is 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.

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Scientific studies demonstrate the sensitivity of BTA and NMP-22 are superior to urinary cytology[1]. Studies affirm the adjunctive value of BTA stat® and NMP-22 in suspected and known bladder cancer in conjunction with cystoscopy. However, false positive results occur more frequently in the presence of hematuria, nephrolithiasis, recent GU instrumentation, inflammation and other urological malignancies. Administration of BCG within 2 years of testing decreases specificity to 28%.

The DNA probe assay has high sensitivity (81%) and specificity (96%) for high grade tumors but lower sensitivity (36-57%) for low grade and stage tumors. The assay specificity approaches that of cytology, and can be utilized in patients recently treated with intravesical bacillus Calmette-Guerin (BCG). This can result in a positive UroVysion® test with a negative study for UC. This assay has also been shown to be useful in predicting tumor recurrence following BCG therapy.

At present the IBCCG has recommended that tumor markers be used in conjunction with cystoscopy. They also concluded that routine screening for bladder cancer is not cost-effective[3]. The US Preventive Services Task Force concluded bladder tumor markers do not have a proven role in screening of asymptomatic patients for early detection of bladder cancer.[3] NCCN, ASCO, and AUA are silent regarding the utilization of these bladder tumor markers.

Surveillance Tests

- **BTA (bladder tumor antigen) stat®** - a qualitative CLIA-waved test that identifies a human complement factor H-related protein produced by several human bladder cell lines
- **The ImmunoCyt™** test is cleared for monitoring bladder cancer recurrence only in conjunction with cytology and cystoscopy. The assay uses fluorescent labeled antibodies to 3 markers (carcinoembryonic antigen, and mucins LDQ10 and M344) commonly found on malignant exfoliated urothelial cells. The ImmunoCyt assay has also been shown to be more sensitive than urine cytology.

LIMITATIONS

Cystoscopy in conjunction with bladder tumor markers is standard practice to evaluate patients with symptoms suggesting bladder cancer and to monitor treated patients for recurrence or progression. Exceptions, such as high grade bladder cancers s/p radical cystectomy, do exist which preclude cystoscopy prior to testing. Testing indications, limitations and frequency do not apply to urine cytology.

Bladder cancer tumor markers performed by any technology, immunoassay, molecular or FISH testing, are not covered for screening of all patients with hematuria. Bladder tumor markers are not expected to be performed until other diagnostic studies fail to identify the etiology of the hematuria. Urine cytology is not considered a bladder tumor marker.

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All other bladder cancer marker assays, including but not limited to the following, regardless of the methodology are considered investigational and not covered by Medicare:

- BCLA-4
- BLCA-1
- Hyaluronic acid
- Hyaluronidase
- Lewis X antigen
- Microsatellite markers
- Quanticyt
- Soluble FAS TATI (tumor associated trypsin inhibitor)
- Soluble e-cadherin
- Survivin
- Telomerase
- UBC™ Rapid Test (urinary bladder cancer test for cytokeratins 8 and 18)

Associated InformationDocumentation Requirements

The medical record must clearly identify the number and frequency of bladder marker testing.

Medical record documentation must be legible, must be maintained in the patient's medical record (hard copy or electronic copy), and must meet the criteria contained in this LCD and be made available to the A/B MAC upon request.

Utilization Guidelines

- Only one bladder cancer test per single date of service (e.g., FISH then reflex cytology) are considered reasonable and necessary.
- For high risk patients with persistent hematuria and a negative FISH assay following a comprehensive diagnostic (no tumor identified) workup, ONE repeat FISH testing in conjunction with cystoscopy is considered reasonable and necessary within 1 year of the original attempted diagnosis.

Follow-up after initial diagnosis/most recent occurrence and treatment

- Maximum of four (4) bladder tumor marker studies per year for years 1-2
- Maximum of three (3) bladder tumor marker studies per year for year 3
- Maximum of two (2) bladder tumor marker studies for year 4 and
- Maximum of one (1) bladder tumor marker studies follow-up annually for up to 15 years.

Medicare Local Coverage Determination Policy

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There is a frequency associated with this test. Please refer to the Limitations or Utilization Guidelines section on previous page(s).

The ICD10 codes listed below are the top diagnosis codes currently utilized by ordering physicians for the limited coverage test highlighted above that are also listed as medically supportive under Medicare's limited coverage policy. **If you are ordering this test for diagnostic reasons that are not covered under Medicare policy, an Advance Beneficiary Notice form is required.**

Code	Description
E34.0	Carcinoid syndrome
C7A.8	Other malignant neuroendocrine tumors
C7A.012	Malignant carcinoid tumor of the ileum
C7A.098	Malignant carcinoid tumors of other sites
Z78.9	Other specified health status
C7A.010	Malignant carcinoid tumor of the duodenum
C7A.011	Malignant carcinoid tumor of the jejunum
C7A.026	Malignant carcinoid tumor of the rectum

Visit **QuestDiagnostics.com/MLCP** to view current limited coverage tests, reference guides, and policy information.

To view the complete policy and the full list of medically supportive codes, please refer to the CMS website reference www.cms.gov ▶

Last updated: 8/17/23