

Policy Name:	Bladder Cancer Screening, Diagnosis and Monitoring using Ancillary Urinary Tests
Effective Date:	8/20/2018

Important Information – Please Read Before Using This Policy

These services may or may not be covered by all Medica plans. Please refer to the member's plan document for specific coverage information. If there is a difference between this general information and the member's plan document, the member's plan document will be used to determine coverage. With respect to Medicare and Minnesota Health Care Programs, this policy will apply unless those programs require different coverage. Members may contact Medica Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions about this Medica coverage policy may call the Medica Provider Service Center toll-free at 1-800-458-5512.

Medica coverage policies are not medical advice. Members should consult with appropriate health care providers to obtain needed medical advice, care and treatment.

Coverage Policy

Ancillary urinary testing for bladder cancer detection is **COVERED** when an FDA-approved test is used as an adjunct to cytology and cystoscopy in patients with signs and symptoms of bladder cancer, for detecting residual bladder cancer in patients with known bladder cancer, or in detecting recurrent bladder cancer in patients with a known history of bladder cancer.

The CxBladder™ test for the detection of bladder cancer, ancillary urinary testing for bladder cancer screening or any ancillary testing that is not FDA approved is investigative and therefore **NOT COVERED**.

Note: This policy is no longer scheduled for routine review of the scientific literature.

Description

Bladder cancer is the fourth most common cancer in men in the United States, and the ninth most common in women. The lifetime probability of developing bladder cancer in the United States is approximately 3.8 percent in men and 1.2 percent in women. Symptoms of bladder cancer include hematuria, dysuria and urgency, all of which are common symptoms of other malignant and benign conditions. Standard treatments for bladder cancer include transurethral resection of the bladder (TURB), intravesical instillation of bacillus Calmette-Guerin (BCG), chemotherapy, cystectomy, and radiotherapy.

Treatment of bladder cancer is complicated by a 50%-70% rate of recurrence in patients with tumors successfully excised via TURB. These cancers progress to higher grades and stages in 15% to 25% of all recurrent cases. For these reasons, patients successfully treated for bladder cancer are monitored at regular intervals for multiple years. The standard for monitoring involves cystoscopy along with cytology of voided urine or bladder washing specimens to detect cancer cells. Cystoscopy is highly sensitive but may miss 10% to 27% of all tumors, particularly carcinoma in situ.

The limitation of cytology has led to the development of several urine-based tests as adjuncts to cystoscopy. A variety of ancillary tests are available. These include, but are not limited to, the following:

- A. Detection of aneuploidy (more than two or less than two copies) of chromosomes 3, 7, 17, and loss of the 9p21 locus. It detects high grade sub-epithelial tumors and carcinoma in situ that can be overlooked with traditional diagnostic methods and have high progression rates to muscle-invasive cancer.

- B. Bladder tumor antigen tests use monoclonal antibodies (mABs) to detect specific proteins in the urine associated with bladder tumors. The BTA *stat* can be used at point-of-care or in the home.
- C. Nuclear matrix protein NMP22 is found in the nuclear matrix of all cell types. However, levels of NMP22 found in the urine in the presence of bladder cancer is often increased by more than 25-fold compared to urine from normal bladders. As with other bladder tumor antigen tests, mABs are used to capture and detect the antigens.
- D. Microsatellite analysis examines short segments of DNA that consist of repeating sequences of 1-6 nucleotides, called microsatellites. Markers identify specific chromosomal or genetic loci that exhibit a genetic pattern consistent with cancerous changes. DNA is amplified using polymerase chain reaction (PCR) performed on blood and urine samples. This is followed by electrophoresis to separate components of the PCR product and allow analysis of DNA for microsatellite instability (MIN) that may indicate presence of cancer.
- E. Telomeres are sequences of DNA that function as “caps” to the ends of chromosomes. Telomeres become shorter after each cell division, eventually causing the cell to stop dividing. Telomerase is an enzyme that allows the telomeres to maintain their length. As a result, cell division continues and a tumor continues to grow. Telomerase is present in 90 percent of cancerous cells. Telomerase tests for bladder cancer are performed on a urine sample using telomeric repeat amplification protocol (TRAP) or reverse transcription (RT) - PCR.
- F. RT - PCR or enzyme-linked immunosorbent assay (ELISA) techniques are used to detect intracellular proteins including survivin or cytokeratin, and hyaluronic acid (HA). Survivin, a cytoplasmic protein that inhibits cell death, is not detectable in most normal adult tissue, but is present in bladder cancer. Cytokeratin and HA are increased in the urine of patients with bladder cancer.
- G. CxBladder™ test measures the expression of 5 genes and converts the gene expression levels to a risk score between 0.00 and 1.00. According to the manufacturer’s website, a normal risk score (< 0.12) has a negative predictive value (NPV) of 97%, while an elevated risk score (0.12 to < 0.23) has an NPV of 94%, and a high risk score (≥ 0.23) has a positive predictive value (PPV) for bladder cancer of 68%.
- H. Other tests include fibronectin immunoassays, matrix metalloproteinase (MMP)-9 immunoassays or zymography, MMP-2 immunoassays or zymography, methylation-specific polymerase chain reaction (MSP), vascular endothelial growth factor (VEGF) immunoassays, Lewis X antigen immunocytology, or 486p3/12 antigen immunocytology.

FDA Approval

All ancillary tests listed below have been approved under a 510(k) process for diagnosis or surveillance of bladder cancer.

- A. Tests for detecting aneuploidy of chromosomes 3, 7, 17, and 9 include:
 - 1. The Vysis™ UroVysion™ Bladder Cancer Recurrence Kit (Vysis Inc.) The UroVysion™ Bladder Cancer Detection Kit (Abbott Molecular Inc.).
- B. Tests for detection of bladder tumor-associated antigens include:
 - 1. Bard® BTA® Stat test (Bard Diagnostic Sciences, Inc.)
 - 3. The Bard® BTA TRAK™ Test (Bard Diagnostic Sciences Inc.)
 - 4. The ImmunoCyt™ (DiagnoCure, Inc.).
- C. Tests for detection of nuclear matrix protein 22 (NMP22) and protein degradation products include:
 - 1. Matritech NMP22® Test Kit (Matritech Inc.)
 - 2. NMP22® BladderChek™ Test (Matritech Inc.)
 - 3. Aura Tek FDP (PerImmune Inc.).

No additional ancillary urinary tests have been approved by the FDA for bladder cancer screening, diagnosis, or monitoring.

CxBladder™ Monitor Test (Pacific Edge Ltd) is a proprietary, laboratory-developed test that does not require FDA approval. The assay is performed in a laboratory facility that observes CLIA regulations and the test is not marketed for general distribution.

Medica Coverage Policy



Prior Authorization

Prior authorization is not required. However, services with specific coverage criteria may be reviewed retrospectively to determine if criteria are being met. Retrospective denial may result if criteria are not met.

Coding Considerations

Use the current applicable CPT/HCPCS code(s). The following codes are included below for informational purposes only, and are subject to change without notice. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement.

CPT Codes:

- 85362 - Fibrin(ogen) degradation (split) products (FDP) (FSP); agglutination slide, semiquantitative
- 86294 - Immunoassay for tumor antigen, quantitative; CA 15-3
- 86386 - Nuclear Matrix Protein 22 (NMP22), qualitative
- 88120 - Cytopathology, in situ hybridization (eg, FISH), urinary tract specimen with morphometric analysis, 3-5 molecular probes, each specimen; manual
- 88121- Cytopathology, in situ hybridization (eg, FISH), urinary tract specimen with morphometric analysis, 3-5 molecular probes, each specimen; using computer-assisted technology

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