UroVysion FISH for Bladder Cancer

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Introduction

UroVysion FISH for bladder cancer is addressed by this guideline.

Procedures addressed

The inclusion of any procedure code in this table does not imply that the code is under management or requires prior authorization. Refer to the specific Health Plan's procedure code list for management requirements.

Procedures addressed by this guideline	Procedure codes
FISH Analysis for Bladder Cancer (UroVysion), Computer-Assisted	88121
FISH Analysis for Bladder Cancer (UroVysion), Manual	88120

Criteria

Introduction

Requests for UroVysion FISH for bladder cancer are reviewed using the following criteria.

- Previous Testing:
  - No repeat UroVysion® testing on the same sample when a result was successfully obtained, AND
- Diagnosis
  - UroVysion is not indicated for the routine evaluation of hematuria or microhematuria. Exceptions may be made for uncertain or equivocal results on standard diagnostic assessments, such as cytology, OR
- Surveillance
  - UroVysion is indicated when the individual has a personal history of bladder cancer, AND
  - The member is being monitored for cancer recurrence, AND
    - Member had been diagnosed with low grade bladder cancer and the results of cytology are equivocal, or

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    - Member had been diagnosed with high grade bladder cancer and the results of cytology are negative or equivocal, AND

- Rendering laboratory is a qualified provider of service per the Health Plan policy

Billing and Reimbursement

Introduction

This section outlines the billing requirements for tests addressed in this guideline. These requirements will be enforced during the case review process whenever appropriate. Examples of requirements may include specific coding scenarios, limits on allowable test combinations or frequency and/or information that must be provided on a claim for automated processing. Any claims submitted without the necessary information to allow for automated processing (e.g. ICD code, place of service, etc.) will not be reimbursable as billed. Any claim may require submission of medical records for post service review.

UroVysion is reimbursable when billed with an ICD code of Z85.51 (Personal history of malignant neoplasm of bladder) or C67.0-C67.9 (Malignant neoplasm of the bladder, range)

UroVysion is not reimbursable when billed with an ICD code in the R31 Hematuria range.

Non-specific procedure codes or any procedure codes that do not accurately describe the test methodology performed are not eligible for reimbursement. For example, 88271 is not a reimbursable code for this test.

What is UroVysion FISH testing for bladder cancer?

Definition

UroVysion™ was developed to be used with current standard diagnostic tools to aid in initial diagnosis of bladder cancer and monitoring for tumor recurrence in previously diagnosed individuals.[1]

- Bladder cancer is one of the most common types of cancer in the U.S., especially among men. Approximately 82,290 new cases of bladder cancer are projected for 2023 (62,420 in men and 19,870 in women).[2] Older individuals (average age 73 years) are most often affected.
- Bladder cancer is categorized as non-muscle invasive disease (NMID) or muscle invasive disease (MID).[3] The majority (≈80%) of bladder cancers are NMID.[4]
- Urothelial carcinoma (UC) accounts for most cases of bladder cancer.[1,3]
    - Most cases of UC are low-grade and easily treated.[1]

  - However, UC has a high risk of recurrence (70%), and individuals must be monitored for several years after treatment.[1]

- Diagnostic monitoring usually consists of regular testing of cells in the urine (cytology).[3,5] Cytology is characterized as having high sensitivity for later stage tumors, but lower sensitivity for low-grade, early-stage tumors (20 to 40%). These early lesions tend to shed few cancer cells into the urine, thus limiting the test's sensitivity.[4] UroVysion FISH (fluorescence in situ hybridization) testing is an alternative to cytology.[1,5]

Test information

Introduction

The UroVysion Bladder Cancer Kit (UroVysion Kit;Abbott Molecular Inc.) uses fluorescence in situ hybridization (FISH) for the analysis of "urine specimens from persons with hematuria who are suspected of having bladder cancer."[6]

UroVysion FISH for Bladder Cancer

The UroVysion FISH for bladder cancer test detects aneuploidy of chromosomes 3, 7, and 17, and deletion of the 9p21 locus, abnormalities often found in individuals with UC.[1,6] The test can be used in conjunction with cystoscopy for initial diagnosis or to monitor progression or recurrence among individuals are already diagnosed with bladder cancer.[6,7]

UroVysion testing can be performed if the cytology returns negative or atypical results.[1,3,5]

Results

The following provides information relevant to UroVysion test results:

- Several studies have shown UroVysion FISH testing to have an overall sensitivity of 71- 85% and nearly 100% sensitivity and specificity for the more rare but serious high-grade UC.[1]
- "If UroVysion results are negative but standard clinical or diagnostic tests (eg, cytology or cystoscopy), are positive, the standard procedures take precedence over the UroVysion test."[6]
- "There will be some bladder cancers whose genetic changes cannot be detected by the UroVysion test. Ta stage solitary tumors smaller than 5 mm could not be detected by UroVysion FISH. UroVysion FISH results are dependent on the amount of tumor cells that are deposited on the slide."[6]

Guidelines and evidence

Introduction

This section includes guidelines and evidence pertaining to UroVysion FISH for bladder cancer.

American Urological Association

The American Urological Association (AUA, 2012) stated the following regarding the management of asymptomatic microhematuria:[8]

- “The use of urine cytology and urine markers (NMP22, BTA-stat, and UroVysion FISH) is NOT recommended as a part of routine evaluation of the AMH [asymptomatic microhematuria] patient. (Recommendation: Evidence Strength C).”

American Urological Association and Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction

The American Urological Association (AUA, 2020) and the Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU, 2020) stated the following in a joint guideline:[9]

- "Clinicians should not use urine cytology or urine-based tumor markers in the initial evaluation of patients with MH [microhematuria]. (Strong Recommendation; Evidence Level: Grade C)"
- "Clinicians may obtain urine cytology for patients with persistent microhematuria after a negative workup who have irritative voiding symptoms or risk factors for carcinoma in situ. (Expert Opinion)"
- Additional comments in the general narrative (non-guideline statements) stated:
    - "While there is insufficient evidence to recommend use of these markers routinely in the evaluation of patients with MH, the potential exists for these markers to improve risk stratification over the clinical variables put forth herein, and thereby improve an individualized approach to MH evaluation."
    - "A prospective randomized trial is currently open that randomizes patients based on clinical risk and marker status (NCT03988309). Patients in the marker arm will have a clinical risk stratification, such that patients with low clinical risk and a negative marker will not have cystoscopy but follow-up only, while those with a positive marker or higher risk based on clinical factors will undergo a standard evaluation with cystoscopy. This marker-based approach will be compared to a standard evaluation in the control arm. Such randomized trials will provide the strength of evidence needed to establish a role for markers in patients with hematuria."

American Urological Association and Society of Urologic Oncology

The American Urological Association (AUA, 2020) and the Society of Urologic Oncology (SUO, 2020) published clinical practice guidelines regarding microscopic hematuria and the management of non-muscle invasive bladder cancer (NMIBC).[10]

For urinary markers utilized after diagnosis of bladder cancer, they stated:[10]

- "In surveillance of NMIBC, a clinician should not use urinary biomarkers in place of cystoscopic evaluation (Strong Recommendation; Evidence Strength: Grade B)"
- "In a patient with a history of low-risk cancer and a normal cystoscopy, a clinician should not routinely use a urinary biomarker or cytology during surveillance. (Expert Opinion)"
- "In a patient with NMIBC, a clinician may use biomarkers to assess response to intravesical BCG (UroVysion FISH) and adjudicate equivocal cytology (UroVysion FISH and ImmunoCyt). (Expert Opinion)"

National Comprehensive Cancer Network

The National Comprehensive Cancer Network (NCCN, 2023) stated the following in regard to surveillance of individuals with a history of UC:[3]

- "Urine molecular tests for urothelial tumor markers are now available. Many of these tests have a better sensitivity for detecting bladder cancer than urinary cytology, but specificity is lower. Considering this, evaluation of urinary urothelial tumor markers may be considered during surveillance of high-risk non– muscle-invasive bladder cancer. However, it remains unclear whether these tests offer additional information that is useful for detection and management of non–muscle-invasive bladder tumors. Therefore, the panel considers this to be a category 2B recommendation."

National Institute for Health and Care Excellence

The National Institute for Health and Care Excellence (NICE, 2015; Reaffirmed 2019) published a guideline regarding the diagnosis and management of bladder cancer. They stated that urinary biomarker tests (such as Urovysion using FISH, ImmunoCyt or a nuclear matrix protein 22 (NMP22) test may be used for the diagnosis of individuals with suspected bladder cancer.[11]

U.S. Food and Drug Administration

The UroVysion testing kit is FDA approved,[12] but reviews and guidelines call for additional study before its clinical use becomes standard procedure.[5]

Selected Relevant Publications

A systematic review of UroVysion was conducted by the Agency for Healthcare Research and Quality (AHRQ).[13] Based on 11 studies that were reviewed, the following were noted by authors:

- Diagnostic testing:
  - The sensitivity of Urovysion to detect bladder cancer among undiagnosed individuals with clinical signs and symptoms was 63% (95% CI, 50% to 75%) and specificity was 87% (95% CI, 79% to 93%).
  - The positive likelihood ratio was 5.02 (95% CI 2.93 to 8.60) (moderate increase in the likelihood of disease). The negative likelihood ratio was 0.42 (95% CI 0.30 to 0.59) (small decrease in likelihood of disease).
- Surveillance testing:
  - For individuals being monitored for cancer recurrence the sensitivity was 55% (95% CI, 36% to 72%; 7 studies) and specificity was 80% (95% CI, 66% to 89%; 6 studies).
  - For evaluation of symptoms, sensitivity was 73% (95% CI, 50% to 88%), based on two studies. Specificity of FISH in evaluation of symptoms was only addressed by one study (95%; 95% CI, 87% to 98%).
- The sensitivity of the test increased with higher tumor stage and grade.

A number of peer-reviewed studies that evaluate the analytical validity, clinical validity, and clinical utility of the UroVysion test are available.[14-31] These studies demonstrate the potential for the assay to help detect bladder cancer. Limitations were noted including small sample size, lack of reporting of precision estimates, and different reference standards for confirming disease.

The UroFollow trial will prospectively evaluate the performance of non-invasive methods of follow-up (including UroVysion) compared with standard of care over a period of 3 years.[31]

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Introduction

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