

Local Coverage Determination (LCD): Lab: Bladder/Urothelial Tumor Markers (L36680)

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Contractor Information

| CONTRACTOR NAME | CONTRACT TYPE | CONTRACT NUMBER | JURISDICTION | STATE(S) |
|------------------------------------|---------------|-----------------|--------------|--------------|
| Noridian Healthcare Solutions, LLC | A and B MAC | 02101 - MAC A | J - F | Alaska |
| Noridian Healthcare Solutions, LLC | A and B MAC | 02102 - MAC B | J - F | Alaska |
| Noridian Healthcare Solutions, LLC | A and B MAC | 02201 - MAC A | J - F | Idaho |
| Noridian Healthcare Solutions, LLC | A and B MAC | 02202 - MAC B | J - F | Idaho |
| Noridian Healthcare Solutions, LLC | A and B MAC | 02301 - MAC A | J - F | Oregon |
| Noridian Healthcare Solutions, LLC | A and B MAC | 02302 - MAC B | J - F | Oregon |
| Noridian Healthcare Solutions, LLC | A and B MAC | 02401 - MAC A | J - F | Washington |
| Noridian Healthcare Solutions, LLC | A and B MAC | 02402 - MAC B | J - F | Washington |
| Noridian Healthcare Solutions, LLC | A and B MAC | 03101 - MAC A | J - F | Arizona |
| Noridian Healthcare Solutions, LLC | A and B MAC | 03102 - MAC B | J - F | Arizona |
| Noridian Healthcare Solutions, LLC | A and B MAC | 03201 - MAC A | J - F | Montana |
| Noridian Healthcare Solutions, LLC | A and B MAC | 03202 - MAC B | J - F | Montana |
| Noridian Healthcare Solutions, LLC | A and B MAC | 03301 - MAC A | J - F | North Dakota |
| Noridian Healthcare Solutions, LLC | A and B MAC | 03302 - MAC B | J - F | North Dakota |
| Noridian Healthcare Solutions, LLC | A and B MAC | 03401 - MAC A | J - F | South Dakota |
| Noridian Healthcare Solutions, LLC | A and B MAC | 03402 - MAC B | J - F | South Dakota |
| Noridian Healthcare Solutions, LLC | A and B MAC | 03501 - MAC A | J - F | Utah |
| Noridian Healthcare Solutions, LLC | A and B MAC | 03502 - MAC B | J - F | Utah |
| Noridian Healthcare Solutions, LLC | A and B MAC | 03601 - MAC A | J - F | Wyoming |
| Noridian Healthcare Solutions, LLC | A and B MAC | 03602 - MAC B | J - F | Wyoming |

LCD Information

Document Information

LCD ID
L36680

Original Effective Date

For services performed on or after 05/16/2017

LCD Title

Revision Effective Date

Lab: Bladder/Urothelial Tumor Markers

For services performed on or after 03/04/2021

Proposed LCD in Comment Period

N/A

Revision Ending Date

N/A

Source Proposed LCD

DL36680

Retirement Date

N/A

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Notice Period Start Date

03/31/2017

Notice Period End Date

05/15/2017

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CMS National Coverage Policy

Title XVIII of the Social Security Act (SSA), §1862(a)(1)(A) allows coverage and payment for only those services that are considered to be reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.

Title XVIII of the Social Security Act, §1862(a)(7) states Medicare will not cover any services or procedures associated with routine physical checkups.

42 CFR §411.15 Particular Services Excluded From Coverage

42 CFR §410.32 Diagnostic X-ray Tests, Diagnostic Laboratory Tests, and Other Diagnostic Tests: Conditions

42 CFR §410.33 Independent Diagnostic Testing Facility

CMS Internet-Only Manual, Publication 100-08, Medicare Program Integrity Manual, Chapter 3, §3.4.1.3, Diagnosis code requirements

Coverage Guidance

Coverage Indications, Limitations, and/or Medical Necessity

INDICATIONS

Gross painless hematuria is often the first manifestation of a 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, and 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 or 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.

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 Bacillus Calmette-Guerin (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 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 markers 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.

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)

Summary of Evidence

NA

Analysis of Evidence (Rationale for Determination)

NA

General Information

Associated Information

Documentation 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/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.

Sources of Information

N/A

Bibliography

1. Polymedco, Inc. 2008. [BTA stat[®]Test](#). Cortlandt, NY.
2. Grossfeld GD, Litwin MS, Wolf JS Jr, et al. Evaluation of asymptomatic microscopic hematuria in adults: The American Urological Association best practice policy part II: Patient evaluation, cytology, voided markers, imaging, cystoscopy, nephrology evaluation, and follow-up. *Urology*. 2001;57(4):604-10.
3. Guide to Clinical Preventive Services, [U.S. Preventive Services Task Force](#) Accessed on January 13, 2021.
4. Lokeshwar VB, Habuchi T, Grossman HB, et al. Bladder tumor markers beyond cytology: International Consensus Panel on bladder tumor markers. *Urology*. 2005;66:35-63.
5. Messing EM, Teot L, Korman H, et al. Performance of urine test in patients monitored for recurrence of bladder cancer: A multicenter study in the United States. *J Urol*. 2005;174(4 pt 1):1238-41.

Revision History Information

| REVISION HISTORY DATE | REVISION HISTORY NUMBER | REVISION HISTORY EXPLANATION | REASON(S) FOR CHANGE |
|-----------------------|-------------------------|--|---|
| 03/04/2021 | R7 | Under CMS National Coverage Policy updated descriptions and added section headings to regulations. Moved sources 1-5 from Sources of Information to Bibliography . NMP-22 [®] and ImmunoCyt [™] was inserted where appropriate throughout the LCD. Formatting, punctuation and typographical errors were corrected throughout the LCD. Acronyms were inserted and defined where appropriate throughout the LCD. | <ul style="list-style-type: none">• Provider Education/Guidance |

| REVISION HISTORY DATE | REVISION HISTORY NUMBER | REVISION HISTORY EXPLANATION | REASON(S) FOR CHANGE |
|-----------------------|-------------------------|---|--|
| | | <p><i>At this time 21st Century Cures Act will apply to new and revised LCDs that restrict coverage which requires comment and notice. This revision is not a restriction to the coverage determination; and, therefore not all the fields included on the LCD are applicable as noted in this policy.</i></p> | |
| 10/01/2019 | R6 | <p>The LCD is revised to remove CPT/HCPCS codes in the Keyword Section of the LCD.</p> <p>At this time 21st Century Cures Act will apply to new and revised LCDs that restrict coverage which requires comment and notice. This revision is not a restriction to the coverage determination; and, therefore not all the fields included on the LCD are applicable as noted in this policy.</p> | <ul style="list-style-type: none"> • Other (The LCD is revised to remove CPT/HCPCS codes in the Keyword Section of the LCD.) |
| 10/01/2019 | R5 | <p>10/01/2019: This LCD is being revised in order to adhere to CMS requirements per chapter 13, section 13.5.1 of the Program Integrity Manual, to remove all coding from LCDs. There has been no change in coverage with this LCD revision. Regulations regarding billing and coding were removed from the CMS National Coverage Policy section of this LCD and placed in the related Billing and Coding: Lab: Bladder/Urothelial Tumor Markers A55029 Article.</p> <p><i>At this time 21st Century Cures Act will apply to new and revised LCDs that restrict coverage which requires comment and notice. This revision is not a restriction to the coverage determination; and, therefore not all the fields included on the LCD are applicable as noted in this policy.</i></p> | <ul style="list-style-type: none"> • Provider Education/Guidance |
| 10/01/2019 | R4 | <p>10/01/2019: At this time 21st Century Cures Act will apply to new and revised LCDs that restrict coverage which requires comment and notice. This revision is not a restriction to the coverage determination; and, therefore not all the fields included on the LCD are applicable as noted in this policy.</p> <p>This LCD was converted to the "no-codes" format.</p> | <ul style="list-style-type: none"> • Revisions Due To Code Removal |

| REVISION HISTORY DATE | REVISION HISTORY NUMBER | REVISION HISTORY EXPLANATION | REASON(S) FOR CHANGE |
|-----------------------|-------------------------|---|--|
| 10/01/2019 | R3 | 10/01/2019: At this time 21st Century Cures Act will apply to new and revised LCDs that restrict coverage which requires comment and notice. This revision is not a restriction to the coverage determination; and, therefore not all the fields included on the LCD are applicable as noted in this policy. | <ul style="list-style-type: none"> Revisions Due To Code Removal |
| 05/16/2017 | R2 | <p>01/30/2019 - At this time 21st Century Cures Act will apply to new and revised LCDs that restrict coverage which requires comment and notice. This revision is not a restriction to the coverage determination; and, therefore not all the fields included on the LCD are applicable as noted in this policy.</p> <p>Added "Lab" to the title of the LCD.</p> | <ul style="list-style-type: none"> Creation of Uniform LCDs With Other MAC Jurisdiction |
| 05/16/2017 | R1 | <p>09/05/2018 - At this time 21st Century Cures Act will apply to new and revised LCDs that restrict coverage which requires comment and notice. This revision is not a restriction to the coverage determination; and, therefore not all the fields included on the LCD are applicable as noted in this policy.</p> <p>LCD revised to add ICD-10-CM codes: C7A.010, C7A.011, C7A.012, C7A.019, C7A.020 , C7A.021, C7A.022, C7A.023, C7A.024, C7A.025, C7A.026, C7A.029, C7A.090, C7A.091, C7A.092, C7A.093, C7A.094, C7A.095, C7A.096, C7B.01, C7B.02, C7B.03, C7B.04 and E34.0.</p> | <ul style="list-style-type: none"> Creation of Uniform LCDs With Other MAC Jurisdiction |

Associated Documents

Attachments

N/A

Related Local Coverage Documents

Article(s)

A55029 - Billing and Coding: Lab: Bladder/Urothelial Tumor Markers

A55458 - Response to Comments: Bladder/Urothelial Tumor Markers

LCD(s)

DL36680

- (MCD Archive Site)

Related National Coverage Documents

N/A

Public Version(s)

Updated on 02/23/2021 with effective dates 03/04/2021 - N/A

Updated on 01/29/2020 with effective dates 10/01/2019 - 03/03/2021

Updated on 11/21/2019 with effective dates 10/01/2019 - N/A

Updated on 10/04/2019 with effective dates 10/01/2019 - N/A

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Keywords

N/A