



BlueCross BlueShield
of Oklahoma

If a conflict arises between a Clinical Payment and Coding Policy and any plan document under which a member is entitled to Covered Services, the plan document will govern. If a conflict arises between a CPCP and any provider contract pursuant to which a provider participates in and/or provides Covered Services to eligible member(s) and/or plans, the provider contract will govern. "Plan documents" include, but are not limited to, Certificates of Health Care Benefits, benefit booklets, Summary Plan Descriptions, and other coverage documents. Blue Cross and Blue Shield of Oklahoma may use reasonable discretion interpreting and applying this policy to services being delivered in a particular case. BCBSOK has full and final discretionary authority for their interpretation and application to the extent provided under any applicable plan documents.

Providers are responsible for submission of accurate documentation of services performed. Providers are expected to submit claims for services rendered using valid code combinations from Health Insurance Portability and Accountability Act approved code sets. Claims should be coded appropriately according to industry standard coding guidelines including, but not limited to: Uniform Billing Editor, American Medical Association, Current Procedural Terminology, CPT® Assistant, Healthcare Common Procedure Coding System, ICD-10 CM and PCS, National Drug Codes, Diagnosis Related Group guidelines, Centers for Medicare and Medicaid Services National Correct Coding Initiative Policy Manual, CCI table edits and other CMS guidelines.

Claims are subject to the code edit protocols for services/procedures billed. Claim submissions are subject to claim review including but not limited to, any terms of benefit coverage, provider contract language, medical policies, clinical payment and coding policies as well as coding software logic. Upon request, the provider is urged to submit any additional documentation.

Urinary Tumor Markers for Bladder Cancer

Policy Number: CPCPLAB038

Version 1.0

Approval Date: April 28, 2025

Plan Effective Date: August 8, 2025

Description

The plan has implemented certain lab management reimbursement criteria. Not all requirements apply to each product. Providers are urged to review Plan documents for eligible coverage for services rendered.

Reimbursement Information:

1. Urinary biomarkers (bladder tumor antigen/BTA test, nuclear matrix protein (NMP22) test, or fluorescence in situ hybridization/FISH UroVysion Bladder Cancer test) **may be reimbursable** in **any** of the following situations:
 - a. As an adjunct in the diagnostic exclusion of bladder cancer for individuals who have an atypical or equivocal cytology;
 - b. As an adjunct in the monitoring of high-risk, non-muscle invasive bladder cancer.
2. As an adjunct to cystoscopy or cytology in the monitoring of individuals with bladder cancer, the use of fluorescence immunocytology (ImmunoCyt/uCyt) **may be reimbursable**.
3. For the evaluation of hematuria, to screen for bladder cancer in asymptomatic individuals, to diagnose bladder cancer in symptomatic individuals, or for any other indications not discussed above, the following tests **are not reimbursable**:
 - a. Urinary biomarkers (bladder tumor antigen/BTA test, nuclear matrix protein (NMP22) test, or fluorescence in situ hybridization/FISH UroVysion Bladder Cancer test);
 - b. Fluorescence immunocytology (ImmunoCyt/uCyt).
4. Any other urinary tumor markers for bladder cancer not mentioned above **are not reimbursable**.

Procedure Codes

The following is not an all-encompassing code list. The inclusion of a code does not guarantee it is a covered service or eligible for reimbursement.

Codes
86294, 86316, 86386, 88120, 88121, 88346, 88350, 0012M, 0013M, 0363U, 0365U, 0366U, 0367U, 0420U, 0452U, 0465U, 0549U

References:

1. Lerner SP, Raghavan, Derek. Overview of the initial approach and management of urothelial bladder cancer. Updated July 29, 2024. <https://www.uptodate.com/contents/overview-of-the-initial-approach-and-management-of-urothelial-bladder-cancer>
2. Hottinger AF, Hormigo A. Serum Biomarkers. In: Schwab M, ed. *Encyclopedia of Cancer*. Springer Berlin Heidelberg; 2011:3390-3394.
3. ACS. Key Statistics for Bladder Cancer. Updated March 12, 2024. <https://www.cancer.org/cancer/types/bladder-cancer/about/key-statistics.html>
4. NCCN. NCCN Guidelines Version 5.2024 Bladder Cancer. Updated October 28, 2024. https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf
5. DeGeorge KC, Holt HR, Hodges SC. Bladder Cancer: Diagnosis and Treatment. 2017;(1532-0650 (Electronic))
6. Perazalla M. Evaluation of hematuria in adults. Updated December 18, 2024. <https://www.uptodate.com/contents/evaluation-of-hematuria-in-adults>
7. Lotan Y, Choueiri T. Clinical presentation, diagnosis, and staging of bladder cancer. Updated February 25, 2025. <https://www.uptodate.com/contents/clinical-presentation-diagnosis-and-staging-of-bladder-cancer>
8. Sutton AJ, Lamont JV, Evans RM, et al. An early analysis of the cost-effectiveness of a diagnostic classifier for risk stratification of haematuria patients (DCRSHP) compared to flexible cystoscopy in the diagnosis of bladder cancer. *PloS one*. 2018;13(8):e0202796. doi:10.1371/journal.pone.0202796
9. Kaufman DS, Shipley WU, Feldman AS. Bladder cancer. *Lancet (London, England)*. Jul 18 2009;374(9685):239-49. doi:10.1016/s0140-6736(09)60491-8
10. Chou R, Dana T. Screening adults for bladder cancer: A review of the evidence for the u.s. preventive services task force. *Annals of Internal Medicine*. 2010;153(7):461-468. doi:10.7326/0003-4819-153-7-201010050-00009
11. Mitra A, Birkman M, Penson D, Cote R. Urine biomarkers for the detection of urothelial (transitional cell) carcinoma of the bladder Updated January 18, 2024. <https://www.uptodate.com/contents/urine-biomarkers-for-the-detection-of-urothelial-transitional-cell-carcinoma-of-the-bladder>
12. Lopez-Beltran A, Cheng L, Gevaert T, et al. Current and emerging bladder cancer biomarkers with an emphasis on urine biomarkers. *Expert Rev Mol Diagn*. Dec 11 2019;1-13. doi:10.1080/14737159.2020.1699791
13. D'Costa JJ, Goldsmith JC, Wilson JS, Bryan RT, Ward DG. A Systematic Review of the Diagnostic and Prognostic Value of Urinary Protein Biomarkers in Urothelial Bladder Cancer. *Bladder cancer (Amsterdam, Netherlands)*. 2016;2(3):301-317. doi:10.3233/blc-160054
14. Lotan Y, Elias K, Svatek RS, et al. Bladder cancer screening in a high risk asymptomatic population using a point of care urine based protein tumor marker. *The Journal of urology*. Jul 2009;182(1):52-7; discussion 58. doi:10.1016/j.juro.2009.02.142
15. Li HT, Duymich CE, Weisenberger DJ, Liang G. Genetic and Epigenetic Alterations in Bladder Cancer. *Int Neurourol J*. Nov 2016;20(Suppl 2):S84-94. doi:10.5213/inj.1632752.376
16. Mahnert B, Tauber S, Kriegmair M, et al. BTA-TRAK--a useful diagnostic tool in urinary bladder cancer? *Anticancer research*. Jul-Aug 1999;19(4a):2615-9.

17. Grossman H, Messing E, Soloway M, et al. Detection of bladder cancer using a point-of-care proteomic assay. *JAMA*. 2005;293(7):810-816. doi:10.1001/jama.293.7.810
18. Zuiverloon TCM, de Jong FC, Theodorescu D. Clinical Decision Making in Surveillance of Non-Muscle-Invasive Bladder Cancer: The Evolving Roles of Urinary Cytology and Molecular Markers. *Oncology (Williston Park, NY)*. Dec 15 2017;31(12):855-62.
19. Abbott. ALERE NMP22® BLADDERCHEK®. <https://www.globalpointofcare.abbott/en/product-details/nmp22-bladderchek.html>
20. Pangea. Features of Bladder CARE™. <https://pangealab.com/bladder-care/>
21. Pangea. Pangea® Laboratory to License Bladder CARE™ Technology from Zymo Research. <https://www.prnewswire.com/news-releases/pangea-laboratory-to-license-bladder-care-technology-from-zymo-research-300800622.html>
22. Nucleix. BLADDER EPICHECK <https://www.nucleix.com/bladder-epicheck/>
23. D'Andrea D, Soria F, Zehetmayer S, et al. Diagnostic accuracy, clinical utility and influence on decision-making of a methylation urine biomarker test in the surveillance of non-muscle-invasive bladder cancer. *BJU Int*. Jun 2019;123(6):959-967. doi:10.1111/bju.14673
24. AroCell. Bladder Cancer Detection. <https://arocell.com/products/oncology/ubc-rapid/>
25. Ecke TH, Weiß S, Stephan C, et al. UBC(®) Rapid Test-A Urinary Point-of-Care (POC) Assay for Diagnosis of Bladder Cancer with a focus on Non-Muscle Invasive High-Grade Tumors: Results of a Multicenter-Study. *Int J Mol Sci*. Dec 2 2018;19(12)doi:10.3390/ijms19123841
26. NICE. URO17 for detecting bladder cancer. Updated February 4, 2021. <https://www.nice.org.uk/advice/mib250/chapter/The-technology>
27. KDx Diagnostics. URO17® A Better test For Better Health. <https://kdxdiagnostics.com/uro17/>
28. Vasdev, Hampson A, Agarwal S, et al. The role of URO17™ biomarker to enhance diagnosis of urothelial cancer in new hematuria patients-First European Data. *BJUI Compass*. Jan 2021;2(1):46-52. doi:10.1002/bco2.50
29. Nonagen Bioscience. Bladder Cancer. <https://www.nonagen.com/products>
30. Pichler R, Fritz J, Tulchiner G, et al. Increased accuracy of a novel mRNA-based urine test for bladder cancer surveillance. *BJU Int*. Jan 2018;121(1):29-37. doi:10.1111/bju.14019
31. D'Elia C, Folchini DM, Mian C, et al. Diagnostic value of Xpert(®) Bladder Cancer Monitor in the follow-up of patients affected by non-muscle invasive bladder cancer: an update. *Ther Adv Urol*. Jan-Dec 2021;13:1756287221997183. doi:10.1177/1756287221997183
32. Piao XM, Jeong P, Kim YH, et al. Urinary cell-free microRNA biomarker could discriminate bladder cancer from benign hematuria. *Int J Cancer*. Jan 15 2019;144(2):380-388. doi:10.1002/ijc.31849
33. Fantony JJ, Longo TA, Gopalakrishna A, et al. Urinary NID2 and TWIST1 methylation to augment conventional urine cytology for the detection of bladder cancer. *Cancer Biomark*. 2017;18(4):381-387. doi:10.3233/cbm-160261

34. Soubra A, Risk MC. Diagnostics techniques in nonmuscle invasive bladder cancer. *Indian journal of urology : IJU : journal of the Urological Society of India*. Oct-Dec 2015;31(4):283-8. doi:10.4103/0970-1591.166449
35. Lotan Y, Roehrborn CG. Sensitivity and specificity of commonly available bladder tumor markers versus cytology: results of a comprehensive literature review and meta-analyses. *Urology*. 2003;61(1):109-118. doi:10.1016/S0090-4295(02)02136-2
36. Breen V, Kasabov N, Kamat AM, et al. A holistic comparative analysis of diagnostic tests for urothelial carcinoma: a study of Cxbladder Detect, UroVysion® FISH, NMP22® and cytology based on imputation of multiple datasets. *BMC medical research methodology*. 2015;15:45-45. doi:10.1186/s12874-015-0036-8
37. Sathianathen NJ, Butaney M, Weight CJ, Kumar R, Konety BR. Urinary Biomarkers in the Evaluation of Primary Hematuria: A Systematic Review and Meta-Analysis. *Bladder cancer (Amsterdam, Netherlands)*. 2018;4(4):353-63.
38. Chou R, Gore JL, Buckley D, et al. Urinary Biomarkers for Diagnosis of Bladder Cancer: A Systematic Review and Meta-analysis. *Ann Intern Med*. Dec 15 2015;163(12):922-31. doi:10.7326/m15-0997
39. Dudley JC, Schroers-Martin J, Lazzareschi DV, et al. Detection and Surveillance of Bladder Cancer Using Urine Tumor DNA. *Cancer Discov*. Apr 2019;9(4):500-509. doi:10.1158/2159-8290.Cd-18-0825
40. Hirasawa Y, Pagano I, Chen R, et al. Diagnostic performance of Oncuria™, a urinalysis test for bladder cancer. *Journal of Translational Medicine*. 2021/04/06 2021;19(1):141. doi:10.1186/s12967-021-02796-4
41. Schmitz-Dräger BJ, Droller M, Lokeshwar VB, et al. Molecular Markers for Bladder Cancer Screening, Early Diagnosis, and Surveillance: The WHO/ICUD Consensus. *Urologia Internationalis*. 2015;94(1):1-24. doi:10.1159/000369357
42. Halpern JA, Chughtai B, Ghomrawi H. Cost-effectiveness of Common Diagnostic Approaches for Evaluation of Asymptomatic Microscopic Hematuria. *JAMA internal medicine*. Jun 2017;177(6):800-807. doi:10.1001/jamainternmed.2017.0739
43. Landaas EJ, Eckel AM, Wright JL, Baird GS, Hansen RN, Sullivan SD. Application of Health Technology Assessment (HTA) to Evaluate New Laboratory Tests in a Health System: A Case Study of Bladder Cancer Testing. *Acad Pathol*. Jan-Dec 2020;7:2374289520968225. doi:10.1177/2374289520968225
44. Meleth S, Reeder-Hayes K, Ashok M, et al. AHRQ Technology Assessments. *Technology Assessment of Molecular Pathology Testing for the Estimation of Prognosis for Common Cancers*. Agency for Healthcare Research and Quality (US); 2014.
45. Tan WS, Tan WP, Tan MY, et al. Novel urinary biomarkers for the detection of bladder cancer: A systematic review. *Cancer Treat Rev*. Sep 2018;69:39-52. doi:10.1016/j.ctrv.2018.05.012
46. Mossanen M, Wang Y, Szymaniak J, et al. Evaluating the cost of surveillance for non-muscle-invasive bladder cancer: an analysis based on risk categories. *World J Urol*. Oct 2019;37(10):2059-2065. doi:10.1007/s00345-018-2550-x
47. Vasdev N, Hampson A, Agarwal S, et al. The role of URO17™ biomarker to enhance diagnosis of urothelial cancer in new hematuria patients—First European Data. *BJUI Compass*. 2021;2(1):46-52. doi:10.1002/bco2.50

48. Davis R, Jones JS, Barocas DA, et al. Diagnosis, evaluation and follow-up of asymptomatic microhematuria (AMH) in adults: AUA guideline. *The Journal of urology*. Dec 2012;188(6 Suppl):2473-81. doi:10.1016/j.juro.2012.09.078
49. Barocas DA, Boorjian SA, Alvarez RD, et al. Microhematuria: AUA/SUFU Guideline. *The Journal of urology*. Oct 2020;204(4):778-786. doi:10.1097/ju.0000000000001297
50. Chang SS, Boorjian SA, Chou R, et al. Diagnosis and Treatment of Non-Muscle Invasive Bladder Cancer: AUA/SUO Guideline. *The Journal of urology*. Oct 2020;196(4):1021-9. doi:10.1016/j.juro.2016.06.049
51. Holzbeierlein J BB, Buckley DI, et al. Diagnosis and Treatment of Non-Muscle Invasive Bladder Cancer: AUA/SUO Guideline: 2024 Amendment. *Journal of Urology [Internet]*. 2024 Apr 1 2024;
52. Holzbeierlein J BB, Buckley DI, et al. Treatment of non-metastatic muscle-invasive bladder cancer: AUA/ASCO/SUO guideline (2017; amended 2020, 2024). *J Urol*. 2024;
53. Chang SS, Bochner BH, Chou R, et al. Treatment of Non-Metastatic Muscle-Invasive Bladder Cancer: AUA/ASCO/ASTRO/SUO Guideline. *The Journal of urology*. Sep 2017;198(3):552-559. doi:10.1016/j.juro.2017.04.086
54. Moyer VA. Screening for bladder cancer: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. Aug 16 2011;155(4):246-51. doi:10.7326/0003-4819-155-4-201108160-00008
55. USPSTF. Bladder Cancer in Adults: Screening. <https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/bladder-cancer-in-adults-screening>
56. Monteiro LL, Witjes JA, Agarwal PK, et al. ICUD-SIU International Consultation on Bladder Cancer 2017: management of non-muscle invasive bladder cancer. 2018:1-10.
57. NCI. Bladder and Other Urothelial Cancers Screening (PDQ®)–Health Professional Version. U.S. Department of Health and Human Services. Accessed 12/12/2024, <https://www.cancer.gov/types/bladder/hp/bladder-screening-pdq>
58. Witjes JA, Bruins HM, Cathomas R, et al. Muscle-invasive and Metastatic Bladder Cancer. <https://doi.org/10.1016/j.eururo.2023.08.016>
59. Babjuk M, Burger M, Capoun O, et al. European Association of Urology Guidelines on Non-muscle-invasive Bladder Cancer (Ta, T1, and Carcinoma in Situ). *European Urology*. 2022;81(1):75-94. doi:10.1016/j.eururo.2021.08.010
60. EAU. EAU Guidelines on Non-muscle Invasive Bladder Cancer. <https://uroweb.org/guidelines/non-muscle-invasive-bladder-cancer>
61. Bhindi B, Kool R, Kulkarni GS, et al. Canadian Urological Association guideline on the management of non-muscle-invasive bladder cancer – Full-text. *Can Urol Assoc J* 2021;
62. Stecca C, Chowdhury D, Blais N, et al. 2024 CUA-GUMOC Expert Report: Management of unresectable locally advanced and metastatic urothelial carcinoma. *Can Urol Assoc J*. 2024;18(12):379-90
63. FDA. 510(k) Summary Information. https://www.accessdata.fda.gov/cdrh_docs/pdf/K964151.pdf
64. FDA. 510(k) Summary Information. https://www.accessdata.fda.gov/cdrh_docs/pdf/K971402.pdf

65. FDA. Premarket Approval.
<https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P940035>
66. FDA. 510(k) Summary.
https://www.accessdata.fda.gov/cdrh_docs/pdf2/K021231.pdf
67. FDA. Premarket Approval.
<https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P030052>
68. FDA. 510(k) number: K994356.
https://www.accessdata.fda.gov/cdrh_docs/pdf/K994356.pdf
69. Darwiche F, Parekh DJ, Gonzalgo ML. Biomarkers for non-muscle invasive bladder cancer: Current tests and future promise. *Indian journal of urology : IJU : journal of the Urological Society of India*. Oct-Dec 2015;31(4):273-82.
doi:10.4103/0970-1591.166448

Policy Update History:

Approval Date	Effective Date; Summary of Revisions
04/28/2025	08/08/2025; Document updated with literature review. Reimbursement information unchanged. Added code 0452U. References revised.
02/04/2025	04/15/2025; Added code 0549U. No other changes.
04/29/2024	01/15/2025: Document updated with literature review. Reimbursement information unchanged. Added codes 0420U and 0465U. References revised.
11/01/2023	11/01/2023: Document updated with literature review. Reimbursement information revised for clarity. References revised; some added, others removed.
11/01/2022	11/01/2022: New policy