

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 New Mexico may use reasonable discretion interpreting and applying this policy to services being delivered in a particular case. BCBSNM 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: February 4, 2025

Plan Effective Date: April 15, 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, 0465U, 0549U

References:

- Abbott. (2023). *ALERE NMP22® BLADDERCHEK®*. Retrieved 12/18/2023 from <https://www.globalpointofcare.abbott/en/product-details/nmp22-bladderchek.html>
- ACS. (2023). *Key Statistics for Bladder Cancer*. <https://www.cancer.org/cancer/bladder-cancer/about/key-statistics.html>
- AroCell. (2023). *Bladder Cancer Detection*. Retrieved 12/18/2023 from <https://arocell.com/products/oncology/ubc-rapid/>
- AUA. (2021). AUA Guideline Amendment: Non-Muscle Invasive Bladder Cancer/Muscle Invasive Bladder Cancer. <https://www.urotoday.com/conference-highlights/aua-2021-program/aua-2021-bladder-cancer/131965-aua-2021-aua-guideline-amendment-non-muscle-invasive-bladder-cancer-muscle-invasive-bladder-cancer.html>
- AUA/SUO. (2020). Diagnosis and Treatment of Non-Muscle Invasive Bladder Cancer: AUA/SUO Joint Guideline (2020). <https://www.auanet.org/guidelines/guidelines/bladder-cancer-non-muscle-invasive-guideline>
- Babjuk, M., Burger, M., Capoun, O., Cohen, D., Compérat, E. M., Dominguez Escrig, J. L., Gontero, P., Liedberg, F., Masson-Lecomte, A., Mostafid, A. H., Palou, J., van Rhijn, B. W. G., Rouprêt, M., Shariat, S. F., Seisen, T., Soukup, V., & Sylvester, R. J. (2022). European Association of Urology Guidelines on Non-muscle-invasive Bladder Cancer (Ta, T1, and Carcinoma in Situ). *European Urology*, 81(1), 75-94. <https://doi.org/10.1016/j.eururo.2021.08.010>
- Barocas, D. A., Boorjian, S. A., Alvarez, R. D., Downs, T. M., Gross, C. P., Hamilton, B. D., Kobashi, K. C., Lipman, R. R., Lotan, Y., Ng, C. K., Nielsen, M. E., Peterson, A. C., Raman, J. D., Smith-Bindman, R., & Souter, L. H. (2020). Microhematuria: AUA/SUFU Guideline. *J Urol*, 204(4), 778-786. <https://doi.org/10.1097/ju.0000000000001297>
- Breen, V., Kasabov, N., Kamat, A. M., Jacobson, E., Suttie, J. M., O'Sullivan, P. J., Kavalieris, L., & Darling, D. G. (2015). 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*, 15, 45-45. <https://doi.org/10.1186/s12874-015-0036-8>
- Chang, S. S., Bochner, B. H., Chou, R., Dreicer, R., Kamat, A. M., Lerner, S. P., Lotan, Y., Meeks, J. J., Michalski, J. M., Morgan, T. M., Quale, D. Z., Rosenberg, J. E., Zietman, A. L., & Holzbeierlein, J. M. (2017). Treatment of Non-Metastatic Muscle-Invasive Bladder Cancer: AUA/ASCO/ASTRO/SUO Guideline. *J Urol*, 198(3), 552-559. <https://doi.org/10.1016/j.juro.2017.04.086>
- Chang, S. S., Boorjian, S. A., Chou, R., Clark, P. E., Daneshmand, S., Konety, B. R., Pruthi, R., Quale, D. Z., Ritch, C. R., Seigne, J. D., Skinner, E. C., Smith, N. D., &

McKiernan, J. M. (2020). Diagnosis and Treatment of Non-Muscle Invasive Bladder Cancer: AUA/SUO Guideline. *J Urol*, 196(4), 1021-1029. <https://doi.org/10.1016/j.juro.2016.06.049>

Chou, R., & Dana, T. (2010). Screening adults for bladder cancer: A review of the evidence for the u.s. preventive services task force. *Annals of Internal Medicine*, 153(7), 461-468. <https://doi.org/10.7326/0003-4819-153-7-201010050-00009>

Chou, R., Gore, J. L., Buckley, D., Fu, R., Gustafson, K., Griffin, J. C., Grusing, S., & Selph, S. (2015). Urinary Biomarkers for Diagnosis of Bladder Cancer: A Systematic Review and Meta-analysis. *Ann Intern Med*, 163(12), 922-931. <https://doi.org/10.7326/m15-0997>

D'Andrea, D., Soria, F., Zehetmayer, S., Gust, K. M., Korn, S., Witjes, J. A., & Shariat, S. F. (2019). 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*, 123(6), 959-967. <https://doi.org/10.1111/bju.14673>

D'Costa, J. J., Goldsmith, J. C., Wilson, J. S., Bryan, R. T., & Ward, D. G. (2016). A Systematic Review of the Diagnostic and Prognostic Value of Urinary Protein Biomarkers in Urothelial Bladder Cancer. *Bladder Cancer*, 2(3), 301-317. <https://doi.org/10.3233/blc-160054>

D'Elia, C., Folchini, D. M., Mian, C., Hanspeter, E., Schwienbacher, C., Spedicato, G. A., Pycha, S., Vjaters, E., Degener, S., Kafka, M., Pycha, A., & Trenti, E. (2021). 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*, 13, 1756287221997183. <https://doi.org/10.1177/1756287221997183>

Darwiche, F., Parekh, D. J., & Gonzalgo, M. L. (2015). Biomarkers for non-muscle invasive bladder cancer: Current tests and future promise. *Indian J Urol*, 31(4), 273-282. <https://doi.org/10.4103/0970-1591.166448>

Davis, R., Jones, J. S., Barocas, D. A., Castle, E. P., Lang, E. K., Leveillee, R. J., Messing, E. M., Miller, S. D., Peterson, A. C., Turk, T. M., & Weitzel, W. (2012). Diagnosis, evaluation and follow-up of asymptomatic microhematuria (AMH) in adults: AUA guideline. *J Urol*, 188(6 Suppl), 2473-2481. <https://doi.org/10.1016/j.juro.2012.09.078>

DeGeorge, K. C., Holt, H. R., & Hodges, S. C. (2017). Bladder Cancer: Diagnosis and Treatment. (1532-0650 (Electronic)). <https://www.aafp.org/pubs/afp/issues/2017/1015/p507.html>

Dudley, J. C., Schroers-Martin, J., Lazzareschi, D. V., Shi, W. Y., Chen, S. B., Esfahani, M. S., Trivedi, D., Chabon, J. J., Chaudhuri, A. A., Stehr, H., Liu, C. L., Lim, H., Costa, H. A., Nabat, B. Y., Sin, M. L. Y., Liao, J. C., Alizadeh, A. A., & Diehn, M. (2019). Detection and Surveillance of Bladder Cancer Using Urine Tumor DNA. *Cancer Discov*, 9(4), 500-509. <https://doi.org/10.1158/2159-8290.Cd-18-0825>

- EAU. (2023). EAU Guidelines on Non-muscle Invasive Bladder Cancer.
https://d56bochluxqnz.cloudfront.net/documents/full-guideline/EAU-Guidelines-on-Non-muscle-Invasive-Bladder-Cancer-2023_2023-03-10-101110_jued.pdf
- Ecke, T. H., Weiß, S., Stephan, C., Hallmann, S., Arndt, C., Barski, D., Otto, T., & Gerullis, H. (2018). 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*, 19(12).
<https://doi.org/10.3390/ijms19123841>
- Fantony, J. J., Longo, T. A., Gopalakrishna, A., Owusu, R., Lance, R. S., Foo, W. C., Inman, B. A., & Abern, M. R. (2017). Urinary NID2 and TWIST1 methylation to augment conventional urine cytology for the detection of bladder cancer. *Cancer Biomark*, 18(4), 381-387. <https://doi.org/10.3233/cbm-160261>
- FDA. (2018). *Devices@FDA*. Retrieved 11/12 from
- Grossman, H., Messing, E., Soloway, M., & et al. (2005). Detection of bladder cancer using a point-of-care proteomic assay. *JAMA*, 293(7), 810-816.
<https://doi.org/10.1001/jama.293.7.810>
- Halpern, J. A., Chughtai, B., & Ghomrawi, H. (2017). Cost-effectiveness of Common Diagnostic Approaches for Evaluation of Asymptomatic Microscopic Hematuria. *JAMA Intern Med*, 177(6), 800-807.
<https://doi.org/10.1001/jamainternmed.2017.0739>
- Hirasawa, Y., Pagano, I., Chen, R., Sun, Y., Dai, Y., Gupta, A., Tikhonenkov, S., Goodison, S., Rosser, C. J., & Furuya, H. (2021). Diagnostic performance of Oncuria™, a urinalysis test for bladder cancer. *Journal of Translational Medicine*, 19(1), 141. <https://doi.org/10.1186/s12967-021-02796-4>
- Hottinger, A. F., & Hormigo, A. (2011). Serum Biomarkers. In M. Schwab (Ed.), *Encyclopedia of Cancer* (pp. 3390-3394). Springer Berlin Heidelberg.
https://doi.org/10.1007/978-3-642-16483-5_5269
- Kaufman, D. S., Shipley, W. U., & Feldman, A. S. (2009). Bladder cancer. *Lancet*, 374(9685), 239-249. [https://doi.org/10.1016/s0140-6736\(09\)60491-8](https://doi.org/10.1016/s0140-6736(09)60491-8)
- Landaas, E. J., Eckel, A. M., Wright, J. L., Baird, G. S., Hansen, R. N., & Sullivan, S. D. (2020). Application of Health Technology Assessment (HTA) to Evaluate New Laboratory Tests in a Health System: A Case Study of Bladder Cancer Testing. *Acad Pathol*, 7, 2374289520968225. <https://doi.org/10.1177/2374289520968225>
- Lerner, S. P., Raghavan, Derek. (2023, 12/18/2023). *Overview of the initial approach and management of urothelial bladder cancer*.
<https://www.uptodate.com/contents/overview-of-the-initial-approach-and-management-of-urothelial-bladder-cancer>

- Li, H. T., Duymich, C. E., Weisenberger, D. J., & Liang, G. (2016). Genetic and Epigenetic Alterations in Bladder Cancer. *Int Neurol J*, 20(Suppl 2), S84-94. <https://doi.org/10.5213/inj.1632752.376>
- Lopez-Beltran, A., Cheng, L., Gevaert, T., Blanca, A., Cimadamore, A., Santoni, M., Massari, F., Scarpelli, M., Raspollini, M. R., & Montironi, R. (2019). Current and emerging bladder cancer biomarkers with an emphasis on urine biomarkers. *Expert Rev Mol Diagn*, 1-13. <https://doi.org/10.1080/14737159.2020.1699791>
- Lotan, Y., & Choueiri, T. (2022, 03/21/2022). *Clinical presentation, diagnosis, and staging of bladder cancer*. <https://www.uptodate.com/contents/clinical-presentation-diagnosis-and-staging-of-bladder-cancer>
- Lotan, Y., Elias, K., Svatek, R. S., Bagrodia, A., Nuss, G., Moran, B., & Sagalowsky, A. I. (2009). Bladder cancer screening in a high risk asymptomatic population using a point of care urine based protein tumor marker. *J Urol*, 182(1), 52-57; discussion 58. <https://doi.org/10.1016/j.juro.2009.02.142>
- Lotan, Y., & Roehrborn, C. G. (2003). Sensitivity and specificity of commonly available bladder tumor markers versus cytology: results of a comprehensive literature review and meta-analyses. *Urology*, 61(1), 109-118. [https://doi.org/10.1016/S0090-4295\(02\)02136-2](https://doi.org/10.1016/S0090-4295(02)02136-2)
- Mahnert, B., Tauber, S., Kriegmair, M., Schmitt, U. M., Hasholzner, U., Reiter, W., Hofmann, K., Schmeller, N., & Stieber, P. (1999). BTA-TRAK--a useful diagnostic tool in urinary bladder cancer? *Anticancer Res*, 19(4a), 2615-2619. <https://pubmed.ncbi.nlm.nih.gov/10470204/>
- Meleth, S., Reeder-Hayes, K., Ashok, M., Clark, R., Funkhouser, W., Wines, R., Hill, C., Shanahan, E., McClure, E., Burson, K., Coker-Schwimmer, M., Garge, N., & Jonas, D. E. (2014). AHRQ Technology Assessments. In *Technology Assessment of Molecular Pathology Testing for the Estimation of Prognosis for Common Cancers*. Agency for Healthcare Research and Quality (US). https://www.ncbi.nlm.nih.gov/books/NBK285410/pdf/Bookshelf_NBK285410.pdf
- Mitra, A., Birkman, M., Penson, D., & Cote, R. (2023, 12/18/2023). *Urine biomarkers for the detection of urothelial (transitional cell) carcinoma of the bladder* <https://www.uptodate.com/contents/urine-biomarkers-for-the-detection-of-urothelial-transitional-cell-carcinoma-of-the-bladder>
- Monteiro, L. L., Witjes, J. A., Agarwal, P. K., Anderson, C. B., Bivalacqua, T. J., Bochner, B. H., Boormans, J. L., Chang, S. S., Domínguez-Escrig, J. L., & McKiernan, J. M. J. W. j. o. u. (2018). ICUD-SIU International Consultation on Bladder Cancer 2017: management of non-muscle invasive bladder cancer. 1-10. <http://urology.stanford.edu/content/dam/sm/urology/JJimages/publications/ICUD-SIU-International-Consultation-on-Bladder-Cancer-2017-management-of-non-muscle-invasive-bladder-cancer.pdf>

- Mossanen, M., Wang, Y., Szymaniak, J., Tan, W. S., Huynh, M. J., Preston, M. A., Trinh, Q. D., Sonpavde, G., Kibel, A. S., & Chang, S. L. (2019). Evaluating the cost of surveillance for non-muscle-invasive bladder cancer: an analysis based on risk categories. *World J Urol*, 37(10), 2059-2065. <https://doi.org/10.1007/s00345-018-2550-x>
- Moyer, V. A. (2011). Screening for bladder cancer: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*, 155(4), 246-251. <https://doi.org/10.7326/0003-4819-155-4-201108160-00008>
- NCCN. (2023a). *Bladder Cancer - Version 3.2023*. https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf
- NCCN. (2023b). NCCN Practice Guidelines: Bladder Cancer Version 3.2023. https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf
- NCI. (2022). *Bladder and Other Urothelial Cancers Screening (PDQ®)–Health Professional Version*. U.S. Department of Health and Human Services. Retrieved 01/29/2023 from <https://www.cancer.gov/types/bladder/hp/bladder-screening-pdq>
- NICE. (2023). URO17 for detecting bladder cancer. <https://www.nice.org.uk/advice/mib250/chapter/The-technology>
- Nonagen Bioscience. (2022). Bladder Cancer. <https://www.nonagen.com/products>
- Nucleix. (2015). *BLADDER EPICHECK* <https://www.nucleix.com/bladder-epicheck/>
- Pangea. (2019). *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>
- Pangea. (2020). Features of Bladder CARE™. <https://www.pangealab.com/bladdercare/>
- Perazalla, M. (2021, 07/09/2021). *Etiology and evaluation of hematuria in adults*. <https://www.uptodate.com/contents/etiology-and-evaluation-of-hematuria-in-adults>
- Piao, X. M., Jeong, P., Kim, Y. H., Byun, Y. J., Xu, Y., Kang, H. W., Ha, Y. S., Kim, W. T., Lee, J. Y., Woo, S. H., Kwon, T. G., Kim, I. Y., Moon, S. K., Choi, Y. H., Cha, E. J., Yun, S. J., & Kim, W. J. (2019). Urinary cell-free microRNA biomarker could discriminate bladder cancer from benign hematuria. *Int J Cancer*, 144(2), 380-388. <https://doi.org/10.1002/ijc.31849>
- Pichler, R., Fritz, J., Tulchiner, G., Klinglmair, G., Soleiman, A., Horninger, W., Klocker, H., & Heidegger, I. (2018). Increased accuracy of a novel mRNA-based urine test

for bladder cancer surveillance. *BJU Int*, 121(1), 29-37.
<https://doi.org/10.1111/bju.14019>

Protean Biodiagnostics. (2021). URO17 is the Most Sensitive and Specific Urine Test for Bladder Cancer. <https://www.proteanbiodx.com/uro17>

Quest. (2020). *Bladder Tumor Antigen DetectR™*.
<https://testdirectory.questdiagnostics.com/test/test-detail/34055/bladder-tumor-antigen-detectr?cc=MASTER>

Sathianathan, N. J., Butaney, M., Weight, C. J., Kumar, R., & Konety, B. R. (2018). Urinary Biomarkers in the Evaluation of Primary Hematuria: A Systematic Review and Meta-Analysis. *Bladder Cancer*, 4(4), 353-363. <https://doi.org/10.3233/blc-180179>

Schmitz-Dräger, B. J., Droller, M., Lokeshwar, V. B., Lotan, Y., Hudson, M. A., van Rhijn, B. W., Marberger, M. J., Fradet, Y., Hemstreet, G. P., Malmstrom, P. U., Ogawa, O., Karakiewicz, P. I., & Shariat, S. F. (2015). Molecular Markers for Bladder Cancer Screening, Early Diagnosis, and Surveillance: The WHO/ICUD Consensus. *Urologia Internationalis*, 94(1), 1-24.
<https://doi.org/10.1159/000369357>

Soubra, A., & Risk, M. C. (2015). Diagnostics techniques in nonmuscle invasive bladder cancer. *Indian J Urol*, 31(4), 283-288. <https://doi.org/10.4103/0970-1591.166449>

Sutton, A. J., Lamont, J. V., Evans, R. M., Williamson, K., O'Rourke, D., Duggan, B., Sagoo, G. S., Reid, C. N., & Ruddock, M. W. (2018). 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*, 13(8), e0202796. <https://doi.org/10.1371/journal.pone.0202796>

Tan, W. S., Tan, W. P., Tan, M. Y., Khetrpal, P., Dong, L., deWinter, P., Feber, A., & Kelly, J. D. (2018). Novel urinary biomarkers for the detection of bladder cancer: A systematic review. *Cancer Treat Rev*, 69, 39-52.
<https://doi.org/10.1016/j.ctrv.2018.05.012>

USPSTF. (2021). *Bladder Cancer in Adults: Screening*.
<https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/bladder-cancer-in-adults-screening>

Vasdev, N., Hampson, A., Agarwal, S., Swamy, R., Chilvers, M., Hampson, A., Jahanfard, S., & Kim, N. (2021). The role of URO17™ biomarker to enhance diagnosis of urothelial cancer in new hematuria patients—First European Data. *BJUI Compass*, 2(1), 46-52. <https://doi.org/10.1002/bco2.50>

Witjes, J. A., Bruins, H. M., Cathomas, R., Compérat, E. M., Cowan, N. C., Gakis, G., Hernández, V., Linares Espinós, E., Lorch, A., Neuzillet, Y., Rouanne, M.,

Thalmann, G. N., Veskimäe, E., Ribal, M. J., & van der Heijden, A. G. (2022). *Muscle-invasive and Metastatic Bladder Cancer*. <https://uroweb.org/guideline/bladder-cancer-muscle-invasive-and-metastatic/>

Zuiverloon, T. C. M., de Jong, F. C., & Theodorescu, D. (2017). Clinical Decision Making in Surveillance of Non-Muscle-Invasive Bladder Cancer: The Evolving Roles of Urinary Cytology and Molecular Markers. *Oncology (Williston Park)*, 31(12), 855-862. <https://www.cancernetwork.com/view/clinical-decision-making-surveillance-nonmuscle-invasive-bladder-cancer-evolving-roles-urinary>

Policy Update History:

Approval Date	Effective Date; Summary of Revisions
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