

## CLINICAL PAYMENT AND CODING POLICY

If a conflict arises between a Clinical Payment and Coding Policy (CPCP) 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. BCBSTX may use reasonable discretion interpreting and applying this policy to services being delivered in a particular case. BCBSTX 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 (HIPAA) approved code sets. Claims should be coded appropriately according to industry standard coding guidelines including, but not limited to: Uniform Billing (UB) Editor, American Medical Association (AMA), Current Procedural Terminology (CPT®), CPT® Assistant, Healthcare Common Procedure Coding System (HCPCS), ICD-10 CM and PCS, National Drug Codes (NDC), Diagnosis Related Group (DRG) guidelines, Centers for Medicare and Medicaid Services (CMS) National Correct Coding Initiative (NCCI) 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**

**Enterprise Medical Policy Committee Approval Date: 1/25/2022**

**Plan Effective Date: May 1, 2022**

#### Description

BCBSTX 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:**

- a. An adjunct in the diagnostic exclusion of bladder cancer for patients who have an atypical or equivocal cytology
  - b. As an adjunct in the monitoring of high-risk, non-muscle invasive bladder cancer
2. The use of fluorescence immunocytology (ImmunoCyt/uCyt) **may be reimbursable** as an adjunct to cystoscopy or cytology in the monitoring of persons with bladder cancer.
  3. Urinary biomarkers (bladder tumor antigen (BTA) test, nuclear matrix protein (NMP22) test, or fluorescence in situ hybridization (FISH) UroVysion Bladder Cancer test) **are not reimbursable** for screening of bladder cancer, evaluation of hematuria, diagnosing bladder cancer in symptomatic individuals, and all other indications.
  4. The use of fluorescence immunocytology (ImmunoCyt/uCyt) **is not reimbursable** in the evaluation of hematuria, diagnosing bladder cancer, or for screening for bladder cancer in asymptomatic persons and all other indications.
  5. Any other urinary tumor markers for bladder cancer not mentioned above **are not reimbursable**

## Procedure Codes

Codes
86294, 86316, 86386, 88120, 88121

## References:

- Abbott. (2020). ALERE NMP22® BLADDERCHEK®. Retrieved from <https://www.globalpointofcare.abbott/en/product-details/nmp22-bladderchek.html>
- Babjuk, M., Bohle, A., Burger, M., Capoun, O., Cohen, D., Comperat, E. M., . . . Zigeuner, R. (2017). EAU Guidelines on Non-Muscle-invasive Urothelial Carcinoma of the Bladder: Update 2016. *Eur Urol*, 71(3), 447-461. doi:10.1016/j.eururo.2016.05.041
- Barocas, D. A., Boorjian, S. A., Alvarez, R. D., Downs, T. M., Gross, C. P., Hamilton, B. D., . . . Souter, L. H. (2020). Microhematuria: AUA/SUFU Guideline. *J Urol*, 204(4), 778-786. doi:10.1097/ju.0000000000001297
- Breen, V., Kasabov, N., Kamat, A. M., Jacobson, E., Suttie, J. M., O'Sullivan, P. J., . . . 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. doi:10.1186/s12874-015-0036-8
- Chang, S. S., Bochner, B. H., Chou, R., Dreicer, R., Kamat, A. M., Lerner, S. P., . . . Holzbeierlein, J. M. (2017). Treatment of Non-Metastatic Muscle-Invasive Bladder Cancer: AUA/ASCO/ASTRO/SUO Guideline. *J Urol*, 198(3), 552-559. doi:10.1016/j.juro.2017.04.086

Chang, S. S., Boorjian, S. A., Chou, R., Clark, P. E., Daneshmand, S., Konety, B. R., . . . McKiernan, J. M. (2016). Diagnosis and Treatment of Non-Muscle Invasive Bladder Cancer: AUA/SUO Guideline. *J Urol*, 196(4), 1021-1029. doi: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. doi:10.7326/0003-4819-153-7-201010050-00009

Chou, R., Gore, J. L., Buckley, D., Fu, R., Gustafson, K., Griffin, J. C., . . . Selph, S. (2015). Urinary Biomarkers for Diagnosis of Bladder Cancer: A Systematic Review and Meta-analysis. *Ann Intern Med*, 163(12), 922-931. doi: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. doi: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. doi:10.3233/blc-160054

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. doi:10.4103/0970-1591.166448

Davis, R., Jones, J. S., Barocas, D. A., Castle, E. P., Lang, E. K., Leveillee, R. J., . . . Weitzel, W. (2012). Diagnosis, evaluation and follow-up of asymptomatic microhematuria (AMH) in adults: AUA guideline. *J Urol*, 188(6 Suppl), 2473-2481. doi: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)).

Dudley, J. C., Schroers-Martin, J., Lazzareschi, D. V., Shi, W. Y., Chen, S. B., Esfahani, M. S., . . . Diehn, M. (2019). Detection and Surveillance of Bladder Cancer Using Urine Tumor DNA. *Cancer Discov*, 9(4), 500-509. doi:10.1158/2159-8290.Cd-18-0825

Ecke, T. H., Weiß, S., Stephan, C., Hallmann, S., Arndt, C., Barski, D., . . . Gerullis, H. (2018). UBC<sup>®</sup> 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). doi:10.3390/ijms19123841

Fantony, J. J., Longo, T. A., Gopalakrishna, A., Owusu, R., Lance, R. S., Foo, W. C., . . . 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. doi:10.3233/cbm-160261

FDA. (2018). Devices@FDA.

FDA. (2021). Devices@FDA.

Fitzmaurice, C., Allen, C., Barber, R. M., Barregard, L., Bhutta, Z. A., Brenner, H., . . . Naghavi, M. (2017). Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life-years for 32 Cancer Groups, 1990 to 2015: A Systematic Analysis for the Global Burden of Disease Study. *JAMA Oncol*, 3(4), 524-548. doi:10.1001/jamaoncol.2016.5688

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. doi: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. doi:10.1001/jamainternmed.2017.0739

Hottinger, A. F., & Hormigo, A. (2011). Serum Biomarkers. In M. Schwab (Ed.), *Encyclopedia of Cancer* (pp. 3390-3394). Berlin, Heidelberg: Springer Berlin Heidelberg.

IDL\_Biotech. (2020). UBC® Rapid. Retrieved from <https://idlbitech.com/products/ubc-rapid/>

Kaufman, D. S., Shipley, W. U., & Feldman, A. S. (2009). Bladder cancer. *Lancet*, 374(9685), 239-249. doi:10.1016/s0140-6736(09)60491-8

Lerner, S. P., Raghavan, Derek. (2020). Overview of the initial approach and management of urothelial bladder cancer. Retrieved from <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 Neurourol J*, 20(Suppl 2), S84-94. doi:10.5213/inj.1632752.376

Lopez-Beltran, A., Cheng, L., Gevaert, T., Blanca, A., Cimadamore, A., Santoni, M., . . . Montironi, R. (2019). Current and emerging bladder cancer biomarkers with an emphasis on urine biomarkers. *Expert Rev Mol Diagn*, 1-13. doi:10.1080/14737159.2020.1699791

Lotan, Y., Choueiri, Toni. (2017). Clinical presentation, diagnosis, and staging of bladder cancer. Retrieved from [https://www.uptodate.com/contents/clinical-presentation-diagnosis-and-staging-of-bladder-cancer?search=bladder%20cancer&source=search\\_result&selectedTitle=1~150&usage\\_type=de\\_fault&display\\_rank=1#H14](https://www.uptodate.com/contents/clinical-presentation-diagnosis-and-staging-of-bladder-cancer?search=bladder%20cancer&source=search_result&selectedTitle=1~150&usage_type=de_fault&display_rank=1#H14)

Lotan, Y., Choueiri, Toni. (2020). Clinical presentation, diagnosis, and staging of bladder cancer. Retrieved from [https://www.uptodate.com/contents/clinical-presentation-diagnosis-and-staging-of-bladder-cancer?search=bladder%20cancer&source=search\\_result&selectedTitle=1~150&usage\\_type=de\\_fault&display\\_rank=1#H14](https://www.uptodate.com/contents/clinical-presentation-diagnosis-and-staging-of-bladder-cancer?search=bladder%20cancer&source=search_result&selectedTitle=1~150&usage_type=de_fault&display_rank=1#H14)

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. doi: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. doi:10.1016/S0090-4295(02)02136-2

Mahnert, B., Tauber, S., Kriegmair, M., Schmitt, U. M., Hasholzner, U., Reiter, W., . . . Stieber, P. (1999). BTA-TRAK--a useful diagnostic tool in urinary bladder cancer? *Anticancer Res*, 19(4a), 2615-2619.

Meleth, S., Reeder-Hayes, K., Ashok, M., Clark, R., Funkhouser, W., Wines, R., . . . Jonas, D. E. (2014). AHRQ Technology Assessments. In *Technology Assessment of Molecular Pathology Testing for the Estimation of Prognosis for Common Cancers*. Rockville (MD): Agency for Healthcare Research and Quality (US).

Mitra, A., Birkman, M., & Penson, D. (2017). Urine biomarkers for the detection of urothelial (transitional cell) carcinoma of the bladder - UpToDate. In M. Ross (Ed.), *UpToDate*. Retrieved from [https://www.uptodate.com/contents/urine-biomarkers-for-the-detection-of-urothelial-transitional-cell-carcinoma-of-the-bladder?source=see\\_link](https://www.uptodate.com/contents/urine-biomarkers-for-the-detection-of-urothelial-transitional-cell-carcinoma-of-the-bladder?source=see_link)

Mitra, A., Birkman, M., Penson, D., & Cote, R. (2019). Urine biomarkers for the detection of urothelial (transitional cell) carcinoma of the bladder - UpToDate. *UpToDate*. Retrieved from [https://www.uptodate.com/contents/urine-biomarkers-for-the-detection-of-urothelial-transitional-cell-carcinoma-of-the-bladder?source=see\\_link](https://www.uptodate.com/contents/urine-biomarkers-for-the-detection-of-urothelial-transitional-cell-carcinoma-of-the-bladder?source=see_link)

Monteiro, L. L., Witjes, J. A., Agarwal, P. K., Anderson, C. B., Bivalacqua, T. J., Bochner, B. H., . . . 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. Retrieved from <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., . . . 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. doi: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. doi:10.7326/0003-4819-155-4-201108160-00008

NACB. (2010). Use of Tumor Markers in Liver, Bladder, Cervical, and Gastric Cancers. Retrieved from <https://www.aacc.org/science-and-practice/practice-guidelines/liver-tumor-markers>

NCCN. (2018). NCCN Clinical Practice Guidelines in Oncology; Bladder Cancer version 5.2018. Retrieved from [https://www.nccn.org/professionals/physician\\_gls/pdf/bladder.pdf](https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf)

NCCN. (2019). Bladder Cancer - Version 1.2020 - November 27, 2019. Retrieved from [https://www.nccn.org/professionals/physician\\_gls/pdf/bladder.pdf](https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf)

NCCN. (2020a). Bladder Cancer Version 3.2020 - January 17, 2020. Retrieved from [https://www.nccn.org/professionals/physician\\_gls/pdf/bladder.pdf](https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf)

NCCN. (2020b). Bladder Cancer Version 6.2020 - July 16, 2020. Retrieved from [https://www.nccn.org/professionals/physician\\_gls/pdf/bladder.pdf](https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf)

NCI. (2018, 03/02/2018). Bladder and Other Urothelial Cancers Screening (PDQ®)—Health Professional Version. PDQ®. Retrieved from <https://www.cancer.gov/types/bladder/hp/bladder-screening-pdq>

NCI. (2020). Bladder and Other Urothelial Cancers Screening (PDQ®)—Health Professional Version. PDQ®. Retrieved from <https://www.cancer.gov/types/bladder/hp/bladder-screening-pdq>

Nucleix. (2015). BLADDER EPICHECK Retrieved from <https://www.nucleix.com/bladder-epicheck/>

Pangea. (2019a). Features of Bladder CARE™. Retrieved from <https://www.pangealab.com/bladdercare/>

Pangea. (2019b). Pangea® Laboratory to License Bladder CARE™ Technology from Zymo Research. Retrieved from <https://www.prnewswire.com/news-releases/pangea-laboratory-to-license-bladder-care-technology-from-zymo-research-300800622.html>

Perazalla, M. (2020). Etiology and evaluation of hematuria in adults. Retrieved from [https://www.uptodate.com/contents/etiology-and-evaluation-of-hematuria-in-adults?topicRef=2989&source=see\\_link](https://www.uptodate.com/contents/etiology-and-evaluation-of-hematuria-in-adults?topicRef=2989&source=see_link)

Piao, X. M., Jeong, P., Kim, Y. H., Byun, Y. J., Xu, Y., Kang, H. W., . . . Kim, W. J. (2019). Urinary cell-free microRNA biomarker could discriminate bladder cancer from benign hematuria. *Int J Cancer*, 144(2), 380-388. doi:10.1002/ijc.31849

Quest. (2020). Bladder Tumor Antigen DetectR™. Retrieved from <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. doi:10.3233/blc-180179

Schmitz-Dräger, B. J., Droller, M., Lokeshwar, V. B., Lotan, Y., Hudson, M. A., van Rhijn, B. W., . . . Shariat, S. F. (2015). Molecular Markers for Bladder Cancer Screening, Early Diagnosis, and Surveillance: The WHO/ICUD Consensus. *Urologia Internationalis*, 94(1), 1-24. doi:10.1159/000369357

Siegel, R. L., Miller, K. D., & Jemal, A. (2017). Cancer Statistics, 2017. *CA Cancer J Clin*, 67(1), 7-30. doi:10.3322/caac.21387

Siegel, R. L., Miller, K. D., & Jemal, A. (2020). Cancer statistics, 2020. *CA Cancer J Clin*, 70(1), 7-30. doi:<https://doi.org/10.3322/caac.21590>

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

Sutton, A. J., Lamont, J. V., Evans, R. M., Williamson, K., O'Rourke, D., Duggan, B., . . . 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. doi:10.1371/journal.pone.0202796

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

USPSTF. (2019). Bladder Cancer in Adults: Screening. Retrieved from <https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/bladder-cancer-in-adults-screening?ds=1&s=bladder%20cancer>

Witjes, J. A., Bruins, H. M., Cathomas, R., Comp erat, E. M., Cowan, N. C., Gakis, G., . . . van der Heijden, A. G. (2020). Muscle-invasive and Metastatic Bladder Cancer. Retrieved from <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.

### Policy Update History:

5/1/2022	New policy
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