Prior Authorization Review Panel
MCO Policy Submission

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Plan: AmeriHealth Caritas Pennsylvania	**Submission Date**: 1/1/2024
Policy Number: ccp.1121	**Effective Date:** 1/2015 **Revision Date:** November 1, 2023
Policy Name: Genetic testing for prostate cancer prognosis	

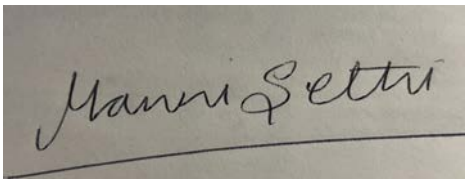
Type of Submission – Check all that apply:

New Policy
x Revised Policy*
Annual Review – No Revisions
Statewide PDL

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any clarifying information for the policy below:

See tracked changes below.

Name of Authorized Individual (Please type or print):	**Signature of Authorized Individual:**
Manni Sethi, MD, MBA, CHCQM	

Genetic testing for prostate cancer prognosis

Clinical Policy ID: CCP.1121

Recent review date: 11/2023

Next review date: 3/2025

Policy contains: Decipher; inherited cancer syndromes; Oncotype; Prolaris; Promark; prostate cancer; risk assessment.

AmeriHealth Caritas Pennsylvania has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas Pennsylvania clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered by AmeriHealth Caritas Pennsylvania when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas Pennsylvania clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas Pennsylvania clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas Pennsylvania will update its clinical policies as necessary. AmeriHealth Caritas Pennsylvania clinical policies are not guarantees of payment.

Coverage policy

Germline genetic testing for prostate cancer is clinically proven and, therefore, may be medically necessary for members with any of the following clinical criteria, and when the testing outcomes will impact care management (National Comprehensive Cancer Network, 2023):

One or more first-, second-, or third-degree relatives with:

- Breast cancer diagnosed at age equal to or greater than 50 years.
- Colorectal or endometrial cancer diagnosed at age equal to or greater than 50 years.
- Male breast cancer at any age.
- Exocrine pancreatic cancer at any age.
- Metastatic, regional, very-high-risk, or high-risk prostate cancer at any age.
- One or more first-degree relatives (parent or sibling) with prostate cancer diagnosed at age equal to or greater than <50 years.
- Example of second degree relatives include grandparents, grandchildren, aunt and uncles, and nephew and nieces.
- Third degree relatives include great-grandparents, great grandchildren and first cousins.
- Three or more first- or second-degree relatives with Lynch syndrome cancers diagnosed at less than 50 years of age, including colorectal, endometrial, gastric, ovarian, exocrine pancreas, upper tract urothelial, glioblastoma, biliary tract, and small intestinal cancer.
- A known family history of familial cancer risk mutation, especially in one of the following genes*: BRCA1, BRCA2, ATM, PALB2, CHEK2, MLH1, MSH2, MSH6, PMS2,* and *EPCAM*

- Ashkenazi Jewish ancestry.

Personal history of:

- Prostate cancer combined with:
- Intermediate-risk prostate cancer with intraductal/cribriform histology.
- Any of the cancers detailed in the family history section above, including exocrine pancreatic cancer, colorectal, gastric, upper tract urothelial, glioblastoma, biliary tract, and small intestinal cancers.

Somatic tumor testing, particularly for homologous recombination gene mutations such as *BRCA1, BRCA2, ATM, PALB2, FANCA, RAD51D, CHEK2,* and *CDK12* is clinically proven and, therefore, may be medically necessary for patients with regional prostate cancer and is essential for those with metastatic conditions. The testing helps in informing treatment decisions for patients with prostate cancer classified as low, intermediate, or high risk, and having a projected life expectancy of a minimum of 10 years, provided the insights from genetic testing will influence the treatment choice (National Comprehensive Cancer Network, 2023).When somatic tumor testing is unsafe or unfeasible, plasma circulating tumor deoxyribonucleic acid (ctDNA) assay is an option preferably collected during biochemical (prostate-specific antigen) and/or radiographic progression in order to maximize diagnostic yield.

Limitations

Genetic testing for a specific gene mutation is limited to once per lifetime. Genetic testing for prostate cancer is not medically necessary for individuals who are not plan members. All other genetic testing for prostate cancer prognosis is not medically necessary, including but not limited to (National Comprehensive Cancer Network, 2023):

- Genetic screening in the general population.
- Members with no personal history of prostate cancer.
- Members younger than age 18 years.

Genetic counseling must be accompanied with a care-coordinating, multidisciplinary team available for genetic counseling, that includes a primary care provider and a geneticist who is a physician or a licensed genetic counselor. If access to a genetic counselor or medical geneticist is not possible, genetic counseling may be initiated by a physician with relevant genetic expertise.

Alternative covered services

- Standard diagnostic and radiographic tests for prostate cancer (e.g., prostate-specific antigen and radionuclide bone scan).
- Genetic counseling.

Background

Prostate cancer is the most common noncutaneous malignancy, and the second-leading cancer cause of death in men (National Cancer Institute, 2022). Prostate cancer is usually slow-growing, and most cases will never become symptomatic during the patient's lifetime. Efforts at early detection with prostate-specific antigen or digital rectal exam and consequent earlier treatment have not resulted in improved health or longevity, and may be harmful. Factors that may increase the risk of prostate cancer include older age (greater than 50 years), a family history of prostate cancer, African American race, high levels of the hormone dihydrotestosterone, and certain dietary factors (vitamin E, folic acid, dairy, and calcium).

Current strategies used to establish prostate cancer prognosis are tumor staging, grading with the Gleason scoring system, and measuring prostate-specific antigen levels to define risk groups. In 2014, the International Society of Urological Pathology (Epstein, 2016) revised the Gleason scoring system into five risk groups based on pathology, and the National Comprehensive Cancer Network (2023 has accepted this new system as a way to better inform treatment decisions. Still, heterogeneity exists within each risk group. Few long-term prognostic models are available to inform decision-making in these patients (Thurtle, 2019). Genetic testing may provide more individualized risk assessment information, particularly regarding the aggressiveness of a tumor.

Prostate cancer is associated with several genes and more than one hundred single nucleotide polymorphisms (National Cancer Institute, 2022). The *BRCA1* gene, *BRCA2* gene, deoxyribonucleic acid mismatch repair genes, and *HOXB13* confer modest to high lifetime risk of prostate cancer. Germline genetic risk markers are appealing as screening biomarkers for their accessibility at any age and their stability over time and in the setting of particular conditions. Men genetically predisposed to developing prostate cancer may benefit from targeted surveillance and targeted gene therapies.

Knowledge of inherited variants from tumor genetic testing may differentiate indolent disease that could be observed safely from aggressive disease that would require treatment. Biomarker testing of blood, urine, and prostate tissue-based molecular assays are commercially available for managing patients with localized prostate cancer (Lamy, 2018). Tumor-based molecular assays for prognosis encompass immunohistochemistry, fluorescence in situ hybridization, enzyme-linked immunosorbent assay, and sequencing methods. Examples of tumor molecular assays available for clinical use in the United States include (Lamy, 2018):

- Decipher — predicts the likelihood that the cancer will metastasize within five years.
- Oncotype DX Genetic Prostate Score — measures tumor aggressiveness and predicts the risk for metastasis and death at 10 years.
- Prolaris — measures tumor aggressiveness and predicts risk of recurrence, metastasis, and death.
- ProMark — measures tumor proteins to provide a personalized prediction that aids in decision to manage cancer with or without aggressive treatment.

Findings

Evaluating the clinical value of a test for screening or diagnosis is the subject of much methodological discussion. The rationale for genetic testing is to provide information that history, physical examination, and any previous testing are considered insufficient to address. The information should be useful to the clinician and to the patient in terms of improving diagnostic certainty, supporting efficacious treatment, and, ultimately, leading to a better clinical outcome.

Available reviews focus on preclinical (laboratory) or observational research, which is still in the process of identifying optimal genetic or molecular markers to identify those men receiving active surveillance who are likely to die from, rather than with, their cancers (Choudhury, 2012; Guo, 2013; Li, 2013; Little, 2012; Yao, 2014). In other words, risk assessment for prostate cancer remains at the hypothesis-generating level (cross-sectional associations of marker concentrations with tumor volume or other intermediate/surrogate endpoints) rather than hypothesis-testing level (trials or cohort studies following tested patients forward in time to assess outcomes). Research confirming that any currently available tests, or those under development, actually impact therapeutic decisions or health outcomes has yet to be published or addressed in systematic reviews.

In 2018, we added one meta-analysis (Cui, 2017), one systematic review (Hamilton, 2017), two evidence-based guidelines from the National Comprehensive Cancer Network on prostate cancer and genetic and familial high-risk assessment for breast and ovarian cancer, and evidence-based and consensus recommendations from the

2017 Philadelphia Prostate Cancer Consensus Conference on genetic testing for inherited prostate cancer risk (Giri, 2018).

Increasing evidence supports an inherited predisposition to prostate cancer with implications for cancer risk assessment for men and their families and targeted treatment of metastatic disease (e.g., early use of platinum chemotherapy). Higher prostate cancer risk is associated with *BRCA* 1/2 mutations (linked to hereditary breast and ovarian cancer syndrome) and *HOXB13* mutations (linked to hereditary prostate cancer), and other gene mutations may be involved. Men with germline *BRCA* 1/2 mutations appear to have more aggressive prostate cancers (e.g., Gleason score ≥ 8), nodal involvement, and distant metastasis compared with noncarriers.

Early studies and guidelines were focused on *BRCA* 1/2 testing, but other genes implicated in prostate cancer predisposition are now available for testing through multigene panels (Giri, 2018). Genetic testing should be analytically and clinically valid, directly impact disease management, and incorporate a tiered panel or targeted test sequence for the minimal number of genes needed to establish the diagnosis. The genetic test should incorporate the genetic spectrum associated with personal and family history of prostate cancer and inherited cancer syndromes, as well as tumor sequencing results. Changes to the coverage policy reflect recommendations on the expanding clinical role of genetic testing in inherited prostate cancer as a complement to current risk assessment strategies (Giri, 2018; National Comprehensive Cancer Network,2023).

In 2019, the National Comprehensive Cancer Network (2019) modified the indications for genetic testing in prostate cancer and expanded the list of genes recommended for germline testing and somatic tumor testing in newly diagnosed men considering active surveillance and in treated men considering adjuvant therapy or treatment of recurrence:

- Germline testing should include the homologous recombination genes *BRCA1*, *BRCA2*, *ATM*, *PALB2*, and *CHEK2* involved in the deoxyribonucleic acid repair pathway. A cancer predisposition next-generation sequencing panel testing, at a minimum including *BRCA2*, *BRCA1*, *ATM*, *CHEK2*, *PALB2*, *MLH1*, *MSH2*, *MSH6*, and *PMS2*, can be considered. Additional genes may be appropriate depending on the clinical context.
- Tumor testing for somatic homologous recombination gene mutations (e.g., *BRCA1*, *BRCA2*, *ATM*, *PALB2*, *FANCA*, *RAD51D*, and *CHEK2*) can be considered in patients with regional or metastatic prostate cancer.
- Tumor testing for deoxyribonucleic acid mismatched repair genes *MLH1*, *MSH2*, *MSH6*, and *PMS2* in patients with regional or metastatic prostate cancer who meet characteristics for Lynch syndrome.
- Multigene molecular testing using Decipher, Oncotype DX Genetic Prostate Score, or Prolaris can be considered for patients with either low or favorable intermediate risk prostate cancer, and life expectancy of at least 10 years.
- The Decipher molecular assay can be considered as part of counseling for risk stratification in patients with prostate-specific antigen resistance/recurrence after radical prostatectomy.

Expanding the list of recommended genes was based in part on the results of a cross-sectional cohort study of 3,607 unselected men with prostate cancer, which highlighted the limitations of using previous versions of National Comprehensive Cancer Network genetic/familial breast and ovarian guidelines and Gleason scores to stratify patients with prostate cancer (Nicolosi, 2019). They identified 674 positive variants in 620 (17.2%) participants, of whom 558 (90%) participants had corresponding family histories. The most frequently detected mutated genes were *BRCA2*, followed by *ATM*, *CHEK2*, and *BRCA1*, representing 11.5% of germline mutations. Approximately 57% of the positive variants detected (386 of 674 variants) were identified in genes not recommended for genetic testing in the previous guidelines, and 229 patients (37%) with the positive variants would not have been referred for genetic testing based on Gleason scores or family history.

A systematic review (Olleik, 2018) of 46 studies that examined the clinical utility of current risk assessment tools supports the clinical utility of the three National Comprehensive Cancer Network-chosen molecular assays to aid in diagnosing prostate cancer and distinguishing indolent from aggressive disease (Oncotype DX Genetic Prostate Score, Decipher, and Prolaris). At diagnosis after a positive biopsy, Decipher and Prolaris aided in the decision to add adjuvant therapy post-prostatectomy. We changed the policy testing criteria and added criteria for molecular testing assays to align with National Comprehensive Cancer Network recommendations.

In 2020, we updated the references, deleted the appendix, deleted the Medicare section, and modified coverage to align with changes in the National Comprehensive Cancer Network (2020) guideline, as follows:

- We separated recommendations for germline and tumor molecular testing. In general, genetic testing is recommended for risk categories in which the results will impact treatment decisions.
- We added the ProMark molecular testing assay to the list of tumor-based molecular testing assays for men with low or favorable intermediate risk disease and life expectancy of at least 10 years.
- We added Prolaris to the list of tumor-based molecular assays for men with unfavorable intermediate and high-risk disease and a life expectancy of at least 10 years.
- For tumor testing for deoxyribonucleic acid mismatched repair genes *MLH1, MSH2, MSH6*, and *PMS2*, we removed the requirement for meeting the characteristics of Lynch syndrome in members with regional or metastatic prostate cancer.

In 2021, we added four systematic reviews to the policy. The systematic review findings from 42 studies (n = 30,407 patients) confirmed the clinical utility of the Decipher genomic classifier in identifying the aggressiveness of prostate cancer, particularly for men with intermediate-risk prostate cancer and post-prostatectomy decision-making (Jairath, 2021). Two systematic reviews examined the prognostic value of androgen receptor splicing variant 7 expression in prostate cancer, but differences in sample sizes and designs, testing assays, and disease characteristics across studies limited the findings (Li, 2021, n = 24 studies; Liu, 2021b, n = 21 studies).

The results of the fourth systematic review (Liu, 2021a, n = 23 studies) suggest plasma cell-free deoxyribonucleic acid concentration may have prognostic value in castration-resistant prostate cancer, but confirmation in larger studies is needed. National Comprehensive Cancer Network (2021) guidance recommended plasma cell-free deoxyribonucleic acid concentration for somatic tumor testing when a metastatic biopsy for molecular and histologic evaluation is not possible, preferably at the time of biochemical or radiographic progression, in order to maximize yield.

In addition, we removed two references, updated the reference list, and added the following indications for germline testing to coverage based on updated National Comprehensive Cancer Network (2021) guidance:

Prostate cancers with cribriform architecture, ductal histology, or intraductal histology.
Suspected germline findings on somatic tumor sequencing.

In 2022, we modified coverage from the latest version of the National Comprehensive Cancer Network guidelines (2022). We added a meta-analysis of 11 studies that compared mutation carrier rates for 11 genes in prostate cancer progressors (n = 3,944) and non-progressors (n = 20,054); the rate for progressors was significantly higher in five of 11 mutations (Shi, 2022). A review of 11 studies of hormone-sensitive prostate cancer patients (n = 1,682) found those with genomic alterations in *AR, TP53*, cell cycle signaling, and *MYC* were more likely to have a poorer clinical outcome (Van der Eecken, 2021).

In 2023, we modified coverage from the latest version of the National Comprehensive Cancer Network guidelines (2023). The American Urological Association and the Society of Urologic Oncology released the early detection of prostate cancer guidelines in 2023 (Wei, 2023). These guidelines noted that polygenic risk scores derived from single nucleotide polymorphisms are used to predict an individual's risk of developing prostate cancer.

Various single nucleotide polymorphism combinations are commercially available, but there's scant evidence guiding which single nucleotide polymorphism panel or polygenic risk score to employ or at which risk level to delineate different screening intensities. We found a systematic review and meta-analysis (Chang, 2023) that aimed to investigate the association of two polymorphisms in the *ESR2* gene (rs1256049 and rs4986938) with susceptibility to prostate cancer).

The ESR2 gene encodes for the estrogen receptor beta (ERβ), which is known to play a role in the progression of hormone-dependent cancers such as prostate cancer. In total, the meta-analysis included 10 articles involving 18,064 cases and 19,556 controls. The findings indicated that the rs1256049 polymorphism of the ESR2 gene might correlate with an increased risk of prostate cancer in people of white ethnicities, while less susceptibility was found in Asians. On the other hand, the rs4986938 polymorphism was not found to be associated with the risk of susceptibility to prostate cancer. In addition, we found a review by Tuffaha (2023) which reviewed 23 guidelines and consensus statements related to prostate cancer genetic testing from 16 organizations. They found a general consensus that men with metastatic prostate cancer should be offered genetic testing, but reached less agreement on testing for men with localized disease. In addition, while genetic testing is routinely recommended, there is still a lack of consensus on who should be tested and how.

References

On September 14, 2023, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were “Prostate cancer, familial” [Supplementary Concept], “prostate cancer,” “risk stratification,” and “genetic tests.” We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

Chang X, Yan Z, Wan H, Wang Y, Han Z, Li J. ESR2 polymorphisms on prostate cancer risk: A systematic review and meta-analysis. *Medicine*. 2023;102(23):e33937. Doi:10.1097/md.0000000000033937.

Choudhury AD, Eeles R, Freedland SJ, et al. The role of genetic markers in the management of prostate cancer. *Eur Urol*. 2012;62(4):577-587. Doi: 10.1016/j.eururo.2012.05.054.

Cui M, Gao XS, Gu X, et al. BRCA2 mutations should be screened early and routinely as markers of poor prognosis: Evidence from 8,988 patients with prostate cancer. *Oncotarget.* 2017;8(25):40222-40232. Doi: 10.18632/oncotarget.16712.

Epstein JI, Egevad L, Amin MB, Delahunt B, Srigley JR, Humphrey PA, Grading Committee. The 2014 International Society of Urological Pathology (ISUP) consensus conference on Gleason grading of prostatic carcinoma: Definition of grading patterns and proposal for a new grading system. *Am J Surg Pathol*. 2016;40(2):244-252. Doi: 10.1097/PAS.0000000000000530.

Giri VN, Knudsen KE, Kelly WK, et al. Role of genetic testing for inherited prostate cancer risk: Philadelphia Prostate Cancer Consensus Conference 2017. *J Clin Oncol*. 2018;36(4):414-424. Doi: 10.1200/jco.2017.74.1173.

Guo Z, Wen J, Kan Q, et al. Lack of association between vitamin D receptor gene FOKL and BSML polymorphisms and prostate cancer risk: An updated meta-analysis involving 21,756 subjects. *Tumor Biol.* 2013;34(5):3189-3200. Doi: 10.1007/s13277-013-0889-6.

Hamilton JG, Abdiwahab E, Edwards HM, Fang ML, Jdayani A, Breslau ES. Primary care providers' cancer genetic testing-related knowledge, attitudes, and communication behaviors: A systematic review and research agenda. *J Gen Intern Med*. 2017;32(3):315-324. Doi: 10.1007/s11606-016-3943-4.

Jairath NK, Dal Pra A, Vince R, Jr., et al. A systematic review of the evidence for the Decipher genomic classifier in prostate cancer. *Eur Urol.* 2021;79(3):374-383. Doi: 10.1016/j.eururo.2020.11.021

Lamy PJ, Allory Y, Gauchez AS, et al. Prognostic biomarkers used for localised prostate cancer management: A systematic review. *Eur Urol Focus.* 2018;4(6):790-803. Doi: 10.1016/j.euf.2017.02.017.

Li Q, Zhu Y. SRD5A2 V89L and A49T polymorphisms and sporadic prostate cancer risk: A meta-analysis. *Mol Biol Rep.* 2013;40(5):3597-3608. Doi: 10.1007/s11033-012-2434-x.

Li Q, Wang Z, Yi J, et al. Clinicopathological characteristics of androgen receptor splicing variant 7 (AR-V7) expression in patients with castration resistant prostate cancer: A systematic review and meta-analysis. *Transl Oncol.* 2021;14(9):101145. Doi: 10.1016/j.tranon.2021.101145.

Little J, Wilson B, Carter R, et al. *Multigene panels in prostate cancer risk assessment. Evidence Report/Technology Assessment No. 209*. (Prepared by the McMaster University Evidence-based Practice Center under contract No. 290-2007-10060-1.) AHRQ Publication No. 12-E020-EF. Rockville, MD. Agency for Healthcare Research and Quality. https://www.ncbi.nlm.nih.gov/books/NBK99070/. Published 2012.

Liu H, Gao Y, Vafaei S, Gu X, Zhong X. The prognostic value of plasma cell-free DNA concentration in the prostate cancer: A systematic review and meta-analysis. *Front Oncol.* 2021;11:599602. Doi: 10.3389/fonc.2021.599602.(a)

Liu RJ, Hu Q, Li SY, et al. The role of androgen receptor splicing variant 7 in predicting the prognosis of metastatic castration-resistant prostate cancer: Systematic review and meta-analysis. *Technol Cancer Res Treat.* 2021;20:15330338211035260. Doi: 10.1177/15330338211035260.(b)

National Cancer Institute. Prostate Cancer Treatment (PDQ®) — Health Professional Version. https://www.cancer.gov/types/prostate/hp/prostate-treatment-pdq. Updated February 2, 2022.

National Comprehensive Cancer Network. Prostate cancer. Version 2.2019. www.nccn.org. Published May 10, 2019.

National Comprehensive Cancer Network. Prostate cancer. Version 1.2020. www.nccn.org. Published May 8, 2020.

National Comprehensive Cancer Network. Prostate cancer. Version 2.2021. www.nccn.org. Published May 7, 2021.

National Comprehensive Cancer Network. Prostate cancer. Version 4.2022. www.nccn.org. Published May 10, 2022.

National Comprehensive Cancer Network. Prostate cancer. Version 4.2023. www.nccn.org. Published September 7, 2023.

Nicolosi P, Ledet E, Yang S, et al. Prevalence of germline variants in prostate cancer and implications for current genetic testing guidelines. *JAMA Oncol.* 2019;5(4):523-528. Doi: 10.1001/jamaoncol.2018.6760.

Olleik G, Kassouf W, Aprikian A, et al. Evaluation of new tests and interventions for prostate cancer management: A systematic review. *J Natl Compr Canc Netw.* 2018;16(11):1340-1351. Doi: 10.6004/jnccn.2018.7055.

Shi Z, Lu L, Resurreccion WK, et al. Association of germline rare pathogenic mutations in guideline-recommended genes with prostate cancer progression: A meta-analysis. *Prostate*. 2022;82(1):107-119. Doi: 10.1002/pros.24252.

Thurtle D, Rossi SH, Berry B, Pharoah P, Gnanapragasam VJ. Models predicting survival to guide treatment decision-making in newly diagnosed primary non-metastatic prostate cancer: A systematic review. *BMJ Open.* 2019;9(6):e029149. Doi: 10.1136/bmjopen-2019-029149.

Tuffaha H, Edmunds K, Fairbairn D, et al. Guidelines for genetic testing in prostate cancer: A scoping review. *Prostate Cancer Prostatic Dis*. 2023. Doi:10.1038/s41391-023-00676-0.

Van der Eecken K, Vanwelkenhuyzen J, Deek MP, et al. Tissue- and blood-derived genomic biomarkers for metastatic hormone-sensitive prostate cancer: A systematic review. *Eur Urol Oncol*. 2021;4(6):914-923. Doi: 10.1016/j.euo.2021.10.005.

Wei JT, Barocas D, Carlsson S, et al. Early detection of prostate cancer: AUA/SUO guideline part i: prostate cancer screening. *J Urol*. 2023;210(1): 46-53. Doi:10.1097/ju.0000000000003491.

Yao YH, Wang H, Li BF, Tang Y. Evaluation of the TMPRSS2:ERG fusion for the detection of prostate cancer: A systematic review and meta-analysis. *Tumor Biol:* 2014; 35(3);2157-2166. Doi: 10.1007/s13277-013-1286-x.

Policy updates

7/2014: initial review date and clinical policy effective date: 1/2015

7/2015: Policy references updated.

7/2016: Policy references updated.

7/2017: Policy references updated.

11/2018: Policy references updated. Policy ID changed. Coverage modified.

11/2019: Policy references updated. Coverage modified.

11/2020: Policy references updated. Coverage modified.

11/2021: Policy references updated. Coverage modified.

11/2022: Policy references updated.

11/2023: Policy references updated.