

Effective November 1, 2023, refer to CMS Manual 100-02, Chapter 16-General Exclusions from Coverage for services included in this policy.



**BlueCross BlueShield
of Alabama**

Name of Blue Advantage Policy:
Systems Pathology in Prostate Cancer

Policy #: 428

Latest Review Date: August 2023

Category: Laboratory

ARCHIVED EFFECTIVE 11/1/2023

BACKGROUND:

Blue Advantage medical policy does not conflict with Local Coverage Determinations (LCDs), Local Medical Review Policies (LMRPs) or National Coverage Determinations (NCDs) or with coverage provisions in Medicare manuals, instructions or operational policy letters. In order to be covered by Blue Advantage the service shall be reasonable and necessary under Title XVIII of the Social Security Act, Section 1862(a)(1)(A). The service is considered reasonable and necessary if it is determined that the service is:

1. *Safe and effective;*
2. *Not experimental or investigational*;*
3. *Appropriate, including duration and frequency that is considered appropriate for the service, in terms of whether it is:*
 - *Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;*
 - *Furnished in a setting appropriate to the patient's medical needs and condition;*
 - *Ordered and furnished by qualified personnel;*
 - *One that meets, but does not exceed, the patient's medical need; and*
 - *At least as beneficial as an existing and available medically appropriate alternative.*

Routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000 which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary by Medicare. Providers should bill **Original Medicare for covered services that are related to **clinical trials** that meet Medicare requirements (Refer to Medicare National Coverage Determinations Manual, Chapter 1, Section 310 and Medicare Claims Processing Manual Chapter 32, Sections 69.0-69.11).*

POLICY:

Blue Advantage will treat the **use of tests utilizing systems pathology that include cellular and biologic features of a tumor** as a **non-covered** benefit and as **investigational**, including use in predicting risk of recurrence in individuals with prostate cancer.

Blue Advantage does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Advantage administers benefits based on the members' contract and medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

DESCRIPTION OF PROCEDURE OR SERVICE:

Predicting risk of recurrence in patients undergoing treatment for prostate cancer is difficult, as it is for most malignancies. Over time, risk models for patients with prostate cancer have evolved from early efforts that relied on grade, stage, and prostate-specific antigen (PSA) levels to complex multivariate models, such as “systems pathology”.

Systems pathology is an approach that combines cellular and biologic features to standard clinical parameters such as age, clinical or pathologic stage, grade, percent of cancer on biopsy cores, and prostate-specific antigen (PSA) or its derivatives. Systems pathology is proposed as a way to estimate the probability of disease progression, either prior to or following prostatectomy.

KEY POINTS:

The policy was last updated with review of literature performed August 11, 2023.

Summary of Evidence

There is a paucity of evidence demonstrating the clinical utility of the use of systems pathology testing. Studies are needed to determine which patients may benefit from this testing, as well as to determine when in the course of diagnosis and treatment the systems pathology assessment should be performed. There also should be further discussion about which outcomes are the best to be used in developing models; there can be substantial differences in models that predict PSA recurrence from those that predict metastatic disease and those that predict death. In addition, models may be needed that evaluate risk following treatments other than radical prostatectomy.

The value of using the systems pathology approach to determine risk is not known based on currently available studies. The impact on net health outcomes is not known and the clinical utility of this testing is not known. The evidence is insufficient to determine the effects of the technology on net health outcomes.

Practice Guidelines and Position Statements

No practice guidelines or position statements are identified.

U.S. Preventive Services Task Force Recommendations
Not applicable.

KEY WORDS:

Prostate Cancer, Progression Prediction, Predicting Recurrence Risk, Systems Pathology, Quantitative Nuclear Morphometry, Prostate, Aureon, Post-op Px, Prostate Px, Prostate Px+, Nadia ProsVue

APPROVED BY GOVERNING BODIES:

Iris Molecular Diagnostics offers the NADiA[®] ProsVue[™] test, which has received FDA 510(k) clearance (k101185). NADiA[®] ProsVue[™] is intended to be used in conjunction with Applied Biosystems 7500 Fast Dx Real-Time PCR Instrument (k082562) and the ProsVue Software.

BENEFIT APPLICATION:

Coverage is subject to member's specific benefits. Group-specific policy will supersede this policy when applicable.

CURRENT CODING:

CPT Codes:

There is no specific CPT code for this test. Various combinations of the following codes may be used to report this testing:

88313	Special stains including interpretation and report; Group II all other (e.g., iron, trichrome), except stain for microorganisms, stains for enzyme constituents, or immunocytochemistry and immunohistochemistry
88323	Consultation and report on referred material requiring preparation of slides
88346	Immunofluorescence, per specimen; initial single antibody stain procedure (Effective 01/01/2016)
88350	each additional single antibody stain procedure (List separately in addition to code for primary procedure)
88399	Unlisted, surgical pathology procedure

REFERENCES:

1. Cordon-Cardo C, Kotsianti A, Verbel DA, et al. Improved prediction of prostate cancer recurrence through systems pathology. *J Clin Invest* 2007; 117(7):1876-83.
2. Donovan MJ, Hamann S, Clayton M, et al. Systems pathology approach for the prediction of prostate cancer progression after radical prostatectomy. *J Clin Oncol* 2008; 26(24):3923-9.
3. Donovan MJ, Khan FM, Bayer-Zubek V et al. A systems-based modelling approach using transurethral resection of the prostate (TURP) specimens yielded incremental prognostic significance to Gleason when predicting long-term outcome in men with localized prostate cancer. *BJU Int* 2012; 109(2):207-13.
4. Donovan MJ, Khan FM, Fernandez G, et al. Personalized prediction of tumor response and cancer progression on prostate needle biopsy. *J Urol* 2009; 182(1):125-32.
5. Donovan MJ, Khan FM, Powell D et al. Postoperative systems models more accurately predict risk of significant disease progression than standard risk groups and a 10-year postoperative nomogram: potential impact on the receipt of adjuvant therapy after surgery. *BJU Int* 2012; 109(1):40-5.
6. Donovan MJ, Osman I, Khan FM. Androgen receptor expression is associated with prostate cancer-specific survival in castrate patients with metastatic disease. *BJU Int* 2010; 105(4):462-7.
7. Eggener SE, Vickers AJ, Serio AM, et al. Comparison of models to predict clinical failure after radical prostatectomy. *Cancer* 2009; 115(2):303-10.
8. IOM (Institute of Medicine). 2011. Clinical Practice Guidelines We Can Trust. Washington, DC: The National Academies Press.
9. Klein EA, Stephenson AJ, Raghavan D, et al. Systems pathology and predicting outcome after radical prostatectomy. *J Clin Oncol* 2008; 26(24):3916-7.
10. Moul JW, Chen DY, Trabulsi EJ, et al. Impact of NADiA ProsVue PSA slope on secondary treatment decisions after radical prostatectomy. *Prostate Cancer Prostatic Dis.* Sep 2014; 17(3):280-285.
11. Moul JW, Lilja H, Semmes OJ et al. NADiA ProsVue prostate-specific antigen slope is an independent prognostic marker for identifying men at reduced risk of clinical recurrence of prostate cancer after radical prostatectomy. *Urology* 2012; 80(6):1319-25.
12. Moul JW, Sarno MJ, McDermed JE, et al. NADiA ProsVue prostate-specific antigen slope, CAPRA-S, and prostate cancer--specific survival after radical prostatectomy. *Urology*. Dec 2014; 84(6):1427-1432.
13. Shariat SF, Karakiewicz PI, Margulis V, et al. Inventory of prostate cancer predictive tools. *Curr Opin Urol* 2008; 18(3):279-96.
14. Veltri RW, Miller MC, Isharwal S, et al. Prediction of prostate-specific antigen recurrence in men with long-term follow-up post prostatectomy using quantitative nuclear morphometry. *Cancer Epidemiol Biomarkers Prev* 2008; 17(1):102-10.

POLICY HISTORY:

Adopted for Blue Advantage, May 2010

Available for comment May 12-June 25, 2010

Medical Policy Group, August 2011

Medical Policy Group, December 2011

Medical Policy Group, June 2012

Medical Policy Group, April 2013

Medical Policy Group, March 2014

Medical Policy Group, March 2015

Medical Policy Group, December 2015

Medical Policy Group, January 2016

Medical Policy Group, August 2019

Medical Policy Group, August 2021: Reviewed by consensus. No new published peer-reviewed literature available that would alter the coverage statement in this policy.

Medical Policy Group, July 2022: Reviewed by consensus. No new published peer-reviewed literature available that would alter the coverage statement in this policy.

Medical Policy Group, August 2023: Reviewed by consensus. No new published peer-reviewed literature available that would alter the coverage statement in this policy.

Medical Policy Group, November 2023: Archived effective 11/1/2023.

This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member's plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield's administration of plan contracts.