Prostate Cancer Screening

Number: 0521

Policy

*Please see amendment for Pennsylvania Medicaid at the end of this CPB.

Aetna considers prostate-specific antigen (PSA) screening a medically necessary preventive service for men aged 40 years and older, and for men under 40 years of age who are at high-risk for prostate cancer. Risk groups include African-American men and men with a family history of prostate cancer.

When used for routine screening, annual PSA screening is considered medically necessary, but additional PSA tests may be considered medically necessary in men with previously elevated PSAs or signs or symptoms of disease.

Aetna considers diagnostic PSA testing medically necessary for men of all ages with signs or symptoms of prostate cancer, and for follow-up of men with prostate cancer.

Aetna considers annual digital rectal examination (DRE) a medically necessary preventive service.

Aetna considers measurement of selenium in the blood or in tissues (such as toenail clippings) experimental and investigational to assess the risk of developing prostate cancer because it has no proven value for this indication.

Policy History

Last Review 05/25/2017
Effective: 02/12/2002
Next Review: 05/24/2018

Review History

Definitions

Additional Information

Clinical Policy Bulletin Notes
Aetna considers the following experimental and investigational for prostate cancer screening because they have no proven value for this indication (not an all-inclusive list):

- Alpha-methylacyl coenzyme A racemase (AMACR)
- Analysis of prostatic fluid electrolyte composition (e.g., citrate, zinc; not an all inclusive list)
- BRAF mutations
- Early prostate cancer antigenE
- Endoglin
- E twenty-six (ETS) gene fusions
- Human glandular kallikrein 2 (hK2) (also known as kallikrein-related peptidase 2 [KLK2])
- Interleukin-6
- MicroRNAs in prostatic fluid/tissue
- Neutrophil gelatinase-associated lipocalin (NGAL)
- Prostate cancer gene 3 (PCA3)
- TMPRSS2:ERG gene fusion
- Transforming growth factor-beta 1

See also CPB 0001 - Transrectal Ultrasound (../1_99/0001.html) and CPB 0352 - Tumor Markers (../300_399/0352.html).

**Note:** Some plans exclude coverage of preventive services. Please check benefit plan descriptions for details. Medically necessary diagnostic PSA testing is covered regardless of whether the member has preventive service benefits.

**Background**

The decision to perform routine prostate cancer screening with digital rectal examination (DRE) or prostate-specific antigen (PSA) is left to the discretion of the clinician. Patients who request screening should be given objective information about the potential benefits and harms of early detection and treatment.
The American Cancer Society (ACS) recommends PSA screening for all men over age 50 and at age 45 for men at higher risk (e.g., men with a family history of prostate cancer and African-American men). Similar recommendations have been issued by the American Urological Association (AUA) and the American College of Radiology. The ACS, however, acknowledges that currently there is no clinical trial evidence that screening for prostate cancer is associated with a reduction in mortality.

The updated ACS guideline for the early detection of prostate cancer (Wolf et al, 2010) recommends both the PSA blood test and DRE should be offered annually, beginning at age 50, to men who have at least a 10-year life expectancy. Men at high-risk (African-American men and men with a strong family of 1 or more first-degree relatives (father, brothers) diagnosed at an early age) should begin testing at age 45. Men at even higher risk, due to multiple first-degree relatives affected at an early age, could begin testing at age 40. Depending on the results of this initial test, no further testing might be needed until age 45. The ACS states that information should be provided to all men about what is known and what is uncertain about the benefits and limitations of early detection and treatment of prostate cancer so that they can make an informed decision about testing. Men who ask their doctor to make the decision on their behalf should be tested. The ACS states that discouraging testing is inappropriate. Furthermore, not offering testing is also inappropriate.

In a review on prostate cancer screening, Ilic and colleagues (2011) concluded that prostate cancer screening did not significantly decrease all-cause or prostate cancer-specific mortality in a combined meta-analysis of 5 randomized controlled trials. Any benefits from prostate cancer screening may take greater than 10 years to accrue; therefore, men who have a life expectancy of less than 10 to 15 years should be informed that screening for prostate cancer is not beneficial and has harms.

The AUA recommends that prostate cancer screening be offered to men over age 50, and at age 40 for men at high-risk, with the physician explaining the uncertain benefits and risks of such screening.

Most professional societies do not recommend routine screening for prostate cancer with DRE or serum tumor markers (e.g., PSA). These include the American Academy of Family Physicians, the U.S. Preventive Services Task Force (USPSTF), the Institute for Clinical Systems Improvement, the Canadian Task Force on the Periodic Health Examination, the American College of Preventive Medicine, the U.S. Office of Technology Assessment, the American Society for Internal Medicine and American College of Physicians, the National Cancer Institute, the Centers for Disease Control and Prevention, and the technology assessment agencies of Canada, England, Sweden, and Australia.

The USPSTF evaluated randomized, controlled trials of the benefits of prostate cancer screening, cohort and cross-sectional studies of the psychological harms of false-positive PSA test results, and evidence on the natural history of PSA-detected prostate cancer and concluded that in men younger than age 75 years, the current evidence is insufficient to determine whether treatment for prostate cancer detected by screening improves health outcomes compared with treatment after clinical detection. In men aged 75 years or older, the USPSTF found no direct evidence of benefits of prostate cancer screening and recommends against screening for prostate cancer in men aged 75 years or older.

If screening is to be performed, the generally accepted approach is to screen with DRE and PSA and to limit screening to men with a life expectancy of greater than 10 years. There is currently insufficient evidence to determine the need and optimal interval for repeat screening or whether PSA thresholds must be adjusted for density, velocity, or age.

Schenk-Braat and Bangma (2006) noted that PSA is currently the most important biochemical marker for the diagnosis of prostate cancer. Because of the limited specificity of PSA, clinically
irrelevant tumors and benign abnormalities are also detected that can potentially lead to over-treatment and the associated physical as well as emotional burden for the patient. Furthermore, PSA is used as an indicator of progression or clinical response following prostate cancer therapy, but the prognostic value of this marker is limited. Ongoing research is examining several alternative markers (e.g., osteoprotegerin, human kallikrein 2, and the gene DD3(PCA3)) that may improve the specificity of current PSA-based diagnostics and the prognostic value of PSA.

Prostate-specific antigen velocity, the yearly rate of increase of PSA, has not been proven to improve the test characteristics of PSA, Schroder and colleagues (2006) stated that PSA-driven screening has been applied to a large part of the male population in many countries. An elevated PSA in secondary screens may indicate benign enlargement of the prostate rather than prostate cancer. In such cases the yearly rate of increase of PSA (PSA velocity [PSAV]) may improve the test characteristics of PSA. These investigators examined if PSAV predict prostate cancer in pre-screened populations. Data from the European Randomized Study of Screening for Prostate Cancer Rotterdam were used to study the issue. Relative sensitivity, relative specificity, and positive predictive value (PPV) were calculated. Logistic regression analysis was used to compare odds ratios for positive biopsies. The relationship between PSAV and parameters of tumor aggressiveness was investigated. A total of 588 consecutive participants were identified who presented at their first screening with PSA values less than 4.0 and who progressed to PSA values greater than 4.0 ng/ml 4 years later were included in this study. None was biopsied in round-1, all were biopsied in round-2. Relative sensitivity and specificity depend strongly on PSAV cut-offs of 0.25 to 1.0 ng/ml/year. The use of PSAV cut-offs did not improve the PPV of the PSA cut-off of 4.0 ng/ml, nor did any of the PSAV cut-offs improve the odds ratio (OR) for identifying prostate cancer with respect to the cut-off value of 4.0 ng/ml. The rate of aggressive cancers seems to increase with increasing PSAV. The authors concluded that PSAV did not improve the detection characteristics of a PSA cut-off of 4.0 ng/ml in secondary screening after 4 years.
Wolters et al (2009) evaluated the value of PSAV in screening for prostate cancer. Specifically, the role of PSAV in lowering the number of unnecessary biopsies and reducing the detection rate of indolent prostate cancer was evaluated. All men included in the study cohort were subjects in the European Randomized Study of Screening for Prostate Cancer (ERSPC), Rotterdam section. During the first and second screening round, a PSA test was performed on 2,217 men, and all underwent a biopsy during the second screening round 4 years later. Prostate specific antigen velocity was calculated and biopsy outcome was classified as benign, possibly indolent prostate cancer, or clinically significant prostate cancer. A total of 441 cases of prostate cancer were detected, 333 were classified as clinically significant and 108 as possibly indolent. The use of PSAV cut-offs reduced the number of biopsies but led to important numbers of missed (indolent and significant) prostate cancer; PSAV was predictive for prostate cancer (OR: 1.28, p < 0.001) and specifically for significant prostate cancer (OR: 1.46, p < 0.001) in uni-variate analyses. However, multi-variate analyses using age, PSA, prostate volume, DRE and transrectal ultrasonography outcome, and previous biopsy (yes/no) showed that PSAV was not an independent predictor of prostate cancer (OR: 1.01, p = 0.91) or significant prostate cancer (OR: 0.87, p = 0.30). The authors concluded that the use of PSAV as a biopsy indicator would miss a large number of clinically significant cases of prostate cancer with increasing PSAV cut-offs. In this study, PSAV was not an independent predictor of a positive biopsy in general or significant prostate cancer on biopsy. Thus, PSAV does not improve the ERSPC screening algorithm.

The role of selenium in cancer prevention has been the subject of recent study and debate. Population studies suggest that people with cancer are more likely to have low selenium levels (measured in the blood or in tissues such as toenail clippings) than healthy matched individuals. However, in most cases it is not clear if low selenium levels are a cause or merely a consequence of disease. Initial evidence from the Nutritional Prevention of Cancer (NPC) trial suggests that selenium supplementation reduces the risk of prostate cancer among men with normal baseline PSA levels and low selenium blood levels.
The ongoing Selenium and Vitamin E Cancer Prevention Trial (SELECT) aims to definitively address the role of selenium in prostate cancer prevention. The study, which spans from 2001 to 2013, will include 32,400 men. Currently, it is unclear if selenium is beneficial in the treatment of prostate cancer or any type of cancer. Measurement of body selenium (e.g., in serum, toenail clippings) has no proven value in the prevention of prostate cancer.

Costello and Franklin (2009) proposed that changes in prostatic fluid composition could provide accurate and reliable biomarkers for the screening of prostate cancer. Most notable is the consistent and significant decrease in citrate and zinc that is associated with the development and progression of prostate cancer. These researchers provided the clinical and physiological basis and the evidence in support of the utility of prostatic fluid analysis as an effective approach for screening/detection of prostate cancer, especially early stage and "at-risk" subjects. The problem of interference from benign prostatic hypertrophy that hampers PSA testing is eliminated in the potential prostatic fluid biomarkers. The potential development of rapid, simple, direct, accurate clinical tests would provide additional advantageous conditions. The authors stated that further exploration and development of citrate, zinc and other electrolytes as prostatic fluid biomarkers are needed to address this critical prostate cancer issue.

A long-term randomized controlled clinical trial found prostate cancer screening had no effect on mortality (Andriole et al, 2009). From 1993 through 2001, investigators randomly assigned 76,693 men at 10 U.S. study centers to receive either annual screening (38,343 subjects) or usual care as the control (38,350 subjects). Men in the screening group were offered annual PSA testing for 6 years and DRE for 4 years. The subjects and health care providers received the results and decided on the type of follow-up evaluation. Usual care sometimes included screening, as some organizations have recommended. The numbers of all cancers and deaths and causes of death were ascertained. In the screening group, rates of compliance were 85 % for PSA testing and 86 % for DRE. Rates of screening in the control group
increased from 40 % in the first year to 52 % in the sixth year for PSA testing and ranged from 41 to 46 % for DRE. After 7 years of follow-up, the incidence of prostate cancer per 10,000 person-years was 116 (2,820 cancers) in the screening group and 95 (2,322 cancers) in the control group (rate ratio, 1.22; 95 % confidence interval [CI]: 1.16 to 1.29). The incidence of death per 10,000 person-years was 2.0 (50 deaths) in the screening group and 1.7 (44 deaths) in the control group (rate ratio, 1.13; 95 % CI: 1.75 to 1.70). The data at 10 years were 67 % complete and consistent with these overall findings. An important limitation of this study is that subjects in the control group underwent considerable screening outside of the clinical trial. An accompanying editorial (Barry, 2009) commented that serial PSA screening has at best a modest effect on prostate cancer mortality during the first decade of follow-up, and that this benefit comes at the cost of substantial over-diagnosis and over-treatment.

Available evidence shows that the majority of men with low-risk prostate tumors receive aggressive treatment, despite the risk of complications. Shao and colleagues (2010) used the Surveillance, Epidemiology and End Results (SEER) database to study the records of 123,934 men over the age of 25 who had newly diagnosed prostate cancer from 2004 to 2006. About 14 % of the men had PSA values lower than 4, generally younger men. In that group, 54 % had low-risk disease that could be safely monitored for progression with little risk. Nonetheless, 75 % of them received aggressive treatment, including a radical prostatectomy and radiation therapy. Among men in that group over the age of 65, in which "watchful waiting" is generally advised for low-risk disease, 66 % had aggressive therapy. In both cases, the percentages were similar to those in the group with PSA levels between 4 and 20.

Mazzola et al (2011) stated that the introduction and widespread adoption of PSA has revolutionized the way prostate cancer is diagnosed and treated. However, the use of PSA has also led to over-diagnosis and over-treatment of prostate cancer resulting in controversy about its use for screening. Prostate specific antigen also has limited predictive accuracy for predicting outcomes after
treatment and for making clinical decisions about adjuvant and salvage therapies. Thus, there is an urgent need for novel biomarkers to supplement PSA for detection and management of prostate cancer. A plethora of promising blood- and urine-based biomarkers have shown promise in early studies and are at various stages of development (human kallikrein 2, early prostate cancer antigen, transforming growth factor-beta 1, interleukin-6, endoglin, prostate cancer gene 3 (PCA3), alpha-methylacyl coenzyme A racemase (AMACR) and E twenty-six (ETS) gene fusions).

Pettersson et al (2012) stated that whether the genomic re-arrangement trans-membrane protease, serine 2 (TMPRSS2):v-ets erythroblastosis virus E26 oncogene homolog (ERG) has prognostic value in prostate cancer is unclear. Among men with prostate cancer in the prospective Physicians' Health and Health Professionals Follow-Up Studies, these researchers identified re-arrangement status by immunohistochemical assessment of ERG protein expression. They used Cox models to examine associations of ERG over-expression with biochemical recurrence and lethal disease (distant metastases or cancer-specific mortality). In a meta-analysis including 47 additional studies, these investigators used random-effects models to estimate associations between re-arrangement status and outcomes. The cohort consisted of 1,180 men treated with radical prostatectomy between 1983 and 2005. During a median follow-up of 12.6 years, 266 men experienced recurrence and 85 men developed lethal disease. These researchers found no significant association between ERG over-expression and biochemical recurrence [hazard ratio (HR), 0.99; 95 % CI: 0.78 to 1.26] or lethal disease (HR, 0.93; 95 % CI: 0.61 to 1.43). The meta-analysis of prostatectomy series included 5,074 men followed for biochemical recurrence (1,623 events), and 2,049 men followed for lethal disease (131 events). TMPRSS2:ERG was associated with stage at diagnosis [risk ratio (RR)(≥T3 vs. T2), 1.23; 95% CI, 1.16-1.30] but not with biochemical recurrence (RR, 1.00; 95 % CI: 0.86 to 1.17) or lethal disease (RR, 0.99; 95 % CI: 0.47 to 2.09). The authors concluded that the findings of this meta-analysis suggested that TMPRSS2:ERG, or ERG over-expression, is associated with tumor stage but does not strongly predict
recurrence or mortality among men treated with radical prostatectomy.

Salagierski et al (2012) stated that widespread PSA screening together with the increase in the number of biopsy cores has led to increased prostate cancer incidence. Standard diagnostic tools still cannot unequivocally predict prostate cancer progression, which often results in a significant over-treatment rate. These investigators presented recent findings on PCA3 and TMPRSS:ERG fusion, and described their clinical implications and performance. The PubMed® database was searched for reports on PCA3 (130 articles), TMPRSS:ERG and ETS fusion (180 publications) since 1999. In recent years advances in genetics and biotechnology have stimulated the development of non-invasive tests to detect prostate cancer. Serum and urine molecular biomarkers have been identified, of which PCA3 has already been introduced clinically. The identification of prostate cancer specific genomic aberrations, i.e., TMPRSS2:ERG gene fusion, might improve diagnosis and affect prostate cancer treatment. The authors concluded that although several recently developed markers are promising, often showing increased specificity for prostate cancer detection compared to that of PSA, their clinical application is limited.

Choudhury et al (2012) noted that despite widespread screening for prostate cancer and major advances in the treatment of metastatic disease, prostate cancer remains the second most common cause of cancer death for men in the Western world. In addition, the use of PSA testing has led to the diagnosis of many potentially indolent cancers, and aggressive treatment of these cancers has caused significant morbidity without clinical benefit in many cases. The recent discoveries of inherited and acquired genetic markers associated with prostate cancer initiation and progression provide an opportunity to apply these findings to guide clinical decision-making. In this review, these investigators discussed the potential use of genetic markers to better define groups of men at high risk of developing prostate cancer, to improve screening techniques, to discriminate indolent versus aggressive disease, and to improve therapeutic strategies in patients with advanced disease. PubMed-based literature
searches and abstracts through January 2012 provided the basis for this literature review. These researchers also examined secondary sources from reference lists of retrieved articles and data presented at recent congresses. Cited review articles were only from the years 2007 to 2012, favoring more recent discussions because of the rapidly changing field. Original research articles were curated based on favoring large sample sizes, independent validation, frequent citations, and basic science directly related to potentially clinically relevant prognostic or predictive markers. In addition, all authors on the manuscript evaluated and interpreted the data acquired. These investigators addressed the use of inherited genetic variants to assess risk of prostate cancer development, risk of advanced disease, and duration of response to hormonal therapies. The potential for using urine measurements such as PCA3 RNA and TMPRSS2-ERG gene fusion to aid screening was discussed. Multiple groups have developed gene expression signatures from primary prostate tumors correlating with poor prognosis, and attempts to improve and standardize these signatures as diagnostic tests were presented. Massive sequencing efforts are underway to define important somatic genetic alterations (amplifications, deletions, point mutations, translocations) in prostate cancer, and these alterations hold great promise as prognostic markers and for predicting response to therapy. These researchers provided a rationale for assessing genetic markers in metastatic disease for guiding choice of therapy and for stratifying patients in clinical trials, and discussed challenges in clinical trial design incorporating the use of these markers. The authors concluded that the use of genetic markers has the potential to aid disease screening, improve prognostic discrimination, and prediction of response to treatment. However, most markers have not been prospectively validated for providing useful prognostic or predictive information or improvement upon clinicopathologic parameters already in use. They stated that significant efforts are underway to develop these research findings into clinically useful diagnostic tests in order to improve clinical decision making.

Measurement of MicroRNAs in Prostatic Fluid/Tissue:

Schubert et al (2016) noted that defining reliable biomarkers is
still a challenge in patients with urological tumors. Because short non-coding RNAs known as microRNAs (miRNAs) regulate diverse important cellular processes, these non-coding RNAs are putative molecular candidates. These researchers provided a critical overview about the current state of miRNAs as biomarkers in urological cancers with respect to prognostic stratification as well as for individual treatment selection. They performed a comprehensive review of the published literature focusing at the clinical relevance of miRNAs in tissues and body fluids of prostate, bladder and kidney cancer. Using electronic database, a total of 91 articles, published between 2009 and 2015, were selected and discussed regarding the robustness of miRNAs as valid biomarkers. A number of miRNAs have been identified with prognostic and predictive relevance in different urologic tumor types. However, the inconsistency of the published results and the lack of multivariate testing in independent cohorts do not allow an introduction into clinical decision making at present. The authors concluded that miRNA-based biomarkers are a promising tool for future personalized risk stratification and response prediction in urological cancers.

Fabris et al (2016) stated that miRNAs control protein expression through the degradation of RNA or the inhibition of protein translation. The miRNAs influence a wide range of biologic processes and are often deregulated in cancer. This family of small RNAs constitutes potentially valuable markers for the diagnosis, prognosis, and therapeutic choices in prostate cancer (PCa) patients, as well as potential drugs (miRNA mimics) or drug targets (anti-miRNAs) in PCa management. These investigators reviewed the currently available data on miRNAs as biomarkers in PCa and as possible tools for early detection and prognosis. A systematic review was performed searching the PubMed database for articles in English using a combination of the following terms: microRNA, miRNA, cancer, prostate cancer, miRNA profiling, diagnosis, prognosis, therapy response, and predictive marker. The authors summarized the existing literature regarding the profiling of miRNA in PCa detection, prognosis, and response to therapy. The articles were reviewed with the main goal of finding a common recommendation that could be translated from bench to bedside in future clinical practice. The
authors concluded that the miRNAs are important regulators of biologic processes in PCa progression. A common expression profile characterizing each tumor subtype and stage has still not been identified for PCa, probably due to molecular heterogeneity as well as differences in study design and patient selection. Moreover, they stated that large-scale studies that should provide additional important information are still missing; further studies, based on common clinical parameters and guidelines, are needed to validate the translational potential of miRNAs in PCa clinical management. Such common signatures are promising in the field and emerge as potential biomarkers. The authors noted that the literature showed that microRNAs hold potential as novel biomarkers that could aid prostate cancer management, but additional studies with larger patient cohorts and common guidelines are needed before clinical implementation.

Furthermore, an UpToDate review on “Screening for prostate cancer” (Hoffman, 2013) does not mention the use of microRNAs as a screening tool for prostate cancer.

**BRAF Mutations:**

Cohn and colleagues (2017) stated that mutations in the BRAF gene have been implicated in several human cancers. The objective of this screening study was to identify patients with solid tumors (other than metastatic melanoma or papillary thyroid cancer) or multiple myeloma harboring activating BRAFV600 mutations for enrollment in a vemurafenib clinical study. Formalin-fixed, paraffin-embedded tumor samples were collected and sent to a central laboratory to identify activating BRAFV600 mutations by bi-directional direct Sanger sequencing. Overall incidence of BRAFV600E mutation in evaluable patients (n = 548) was 3% (95% CI: 1.7 to 4.7): 11% in colorectal tumors (n = 75), 6% in biliary tract tumors (n = 16), 3% in non-small cell lung cancers (n = 71), 2% in other types of solid tumors (n = 180), and 3% in multiple myeloma (n = 31). There were no BRAFV600 mutations in this cohort of patients with ovarian tumors (n = 68), breast cancer (n = 86), or PCa (n = 21). The authors noted that BRAF mutations have been identified in up to 10% of Asian patients with PCa, but appeared to be rare among Caucasian.
patients. The finding of no mutations among 21 patients with PCa is also consistent with data from the COSMIC database, showing documented BRAF mutations in approximately 1% of almost 2,500 sequenced samples.

**Neutrophil Gelatinase-Associated Lipocalin:**

Muslu and colleagues (2017) noted that PSA with DRE is used for diagnosis of PCa, where definite diagnosis can only be made by prostate biopsy. Recently neutrophil gelatinase-associated lipocalin (NGAL), a lipocalin family member glycoprotein, come into prominence as a cancer biomarker. In a prospective study, these researchers tested serum NGAL as a diagnostic biomarker for PCa and for differentiation of PCa from benign prostatic hyperplasia (BPH). A total of 90 patients who underwent transrectal ultrasound (TRUS)-guided 12-core prostate biopsy between May 2015 and September 2015 were evaluated. Histopathologically diagnosed 45 PCa and 45 BPH patients were enrolled in this study. Serum NGAL and PSA levels of all participants were measured, then these data were evaluated by statistical programs. When sensitivity fixed to 80% specificity of NGAL was better than PSA (49% and 31%, respectively). Receiver operating characteristic (ROC) curve analysis showed that NGAL alone or its combined use with PSA exhibited better area under curve (AUC) results than PSA alone (0.662, 0.693, and 0.623, respectively). The authors concluded that NGAL gave promising results such as increased sensitivity and a better AUC values in order to distinguish PCa from BPH. They stated that NGAL showed a potential to be a non-invasive biomarker which may decrease the number of unnecessary biopsies; more studies are needed to define more accurate cut-off values for both NGAL alone and PSA-NGAL combination; and more accurate results can be achieved by increasing the number of cases.
### CPT codes covered if selection criteria are met:

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<td>84152</td>
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### CPT codes not covered for indications listed in the CPB:

#### PCA3:

- 84255 Chemistry, Selenium

#### TMPRSS2:ERG gene fusion, Measurement of microRNAs in prostatic fluid/tissue:

- No specific code

### CPT codes not covered for indications listed in the CPB:

- 81313 PCA3/KLK3 (prostate cancer antigen 3 [non-protein coding]/kallikrein-related peptidase 3 [prostate specific antigen]) ratio (eg, prostate cancer)
- 81539 Oncology (high-grade prostate cancer), biochemical assay of four proteins (Total PSA, Free PSA, Intact PSA, and human kallikrein-2 [hK2]), utilizing plasma or serum, prognostic algorithm reported as a probability score

### Other CPT codes related to the CPB:

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### HCPCS codes covered if selection criteria are met:

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ICD-10 codes covered if selection criteria are met:

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<tr>
<td>Z85.46</td>
<td>Personal history of malignant neoplasm of prostate</td>
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</table>

The above policy is based on the following references:


15. Harris R, Lohr KN. Screening for prostate cancer: An update of the evidence for the U.S. Preventive Services Task


28. University of Michigan Health System. Adult preventive

29. Medical Services Advisory Committee (MSAC). Prostate specific antigen (PSA) near patient testing for diagnosis and management of prostate cancer. MSAC Application 1068. Canberra, ACT: MSAC; 2005.


39. van den Brandt PA, Zeegers MP, Bode P, Goldbohm A. Toenail selenium levels and the subsequent risk of prostate cancer: A prospective Cohort study. Cancer Epidemiol


50. Andriole GL, Crawford ED, Grubb RL 3rd, et al; PLCO Project Team. Mortality results from a randomized prostate-cancer...


64. Hoffman RM. Screening for prostate cancer. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed March 2015.


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AETNA BETTER HEALTH® OF PENNSYLVANIA

Amendment to
Aetna Clinical Policy Bulletin Number: 0521 Prostate Cancer Screening

There are no amendments for Medicaid.

www.aetnabetterhealth.com/pennsylvania
revised 07/18/2017