PHP_7.01.121	Saturation Biopsy for Diagnosis, Staging, and Management of Prostate Cancer		
Original Policy Date:	December 1, 2025	**Effective Date:**	December 1, 2025
Section:	7.0 Surgery	**Page:**	Page 1 of 13

State Guidelines

As of the publication of this policy, there are no applicable Medi-Cal guidelines (Provider Manual or All Plan Letter). Please refer to the Policy Statement section below.

Policy Statement

In the absence of any State Guidelines, please refer to the criteria below.

I. Saturation biopsy is considered **investigational** in the diagnosis, staging, and management of prostate cancer.

Policy Guidelines

Saturation biopsy is generally considered obtaining more than 20 biopsy tissue cores from the prostate in a systematic manner; it is occasionally defined as obtaining more than 18 biopsy tissue cores.

Coding

See the Codes table for details.

Description

Saturation biopsy of the prostate, in which more cores are obtained than by standard biopsy protocol, has been proposed in the diagnosis (for initial or repeat biopsy), staging, and management of individuals with prostate cancer.

Summary of Evidence

For individuals who have suspected prostate cancer who receive initial saturation biopsy, the evidence includes randomized controlled trials (RCTs), observational studies, and systematic reviews. Relevant outcomes are overall survival (OS), disease-specific survival, test accuracy, and treatment-related morbidity. A 2013 systematic review found higher rates of cancer detection with saturation biopsy than with extended biopsy overall, but, in the subgroup of men with prostate-specific antigen (PSA) levels less than 10 ng/mL, the degree of difference was small and possibly not clinically significant. Health outcomes (e.g., survival rate) were not reported. Although several studies were published after the systematic review, none showed that initial saturation biopsy improved the detection of clinically significant cancers and none reported progression or survival outcomes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have suspected prostate cancer receive repeat saturation biopsy, the evidence includes observational studies and a systematic review. Relevant outcomes are OS, disease-specific survival, test accuracy, and treatment-related morbidity. Several studies have compared saturation

with standard prostate biopsies in the repeat biopsy setting and have found significantly higher detection rates with saturation biopsy. However, at least 1 study found that about one-third of the positive findings with saturation biopsy were clinically insignificant cancers. Moreover, studies of saturation biopsy as the repeat prostate biopsy strategy focused on cancer detection rates and did not report health outcomes (e.g., progression or survival). Evidence is lacking as to whether saturation biopsy leads to improved health outcomes, including the possibility of detecting clinically insignificant cancers, which could lead to unnecessary treatment. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have prostate cancer and are candidates for active surveillance who receive saturation biopsy, the evidence includes 2 nonrandomized comparative studies. Relevant outcomes are OS, disease-specific survival, test accuracy, and treatment-related morbidity. Both studies retrospectively compared standard biopsy with saturation biopsy for selecting patients for active surveillance; neither found that saturation biopsy improved the ability to select patients. In 1 study, biopsy method was not a significant predictor of upstaging and, in the other study, biopsy method was not significantly associated with selecting patients with a high Gleason score. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Additional Information
Not applicable.

Related Policies

- N/A

Benefit Application

Blue Shield of California Promise Health Plan is contracted with L.A. Care Health Plan for Los Angeles County and the Department of Health Care Services for San Diego County to provide Medi-Cal health benefits to its Medi-Cal recipients. In order to provide the best health care services and practices, Blue Shield of California Promise Health Plan has an extensive network of Medi-Cal primary care providers and specialists. Recognizing the rich diversity of its membership, our providers are given training and educational materials to assist in understanding the health needs of their patients as it could be affected by a member's cultural heritage.

The benefit designs associated with the Blue Shield of California Promise Medi-Cal plans are described in the Member Handbook (also called Evidence of Coverage).

Regulatory Status

Saturation biopsy is a surgical procedure and, as such, is not subject to regulation by the U.S. Food and Drug Administration.

Health Equity Statement

Blue Shield of California Promise Health Plan's mission is to transform its health care delivery system into one that is worthy of families and friends. Blue Shield of California Promise Health Plan seeks to advance health equity in support of achieving Blue Shield of California Promise Health Plan's mission.

Blue Shield of California Promise Health Plan ensures all Covered Services are available and accessible to all members regardless of sex, race, color, religion, ancestry, national origin, ethnic group identification, age, mental disability, physical disability, medical condition, genetic information,

marital status, gender, gender identity, or sexual orientation, or identification with any other persons or groups defined in Penal Code section 422.56, and that all Covered Services are provided in a culturally and linguistically appropriate manner.

Rationale

Background

Prostate Cancer

Prostate cancer is common and is the second leading cause of cancer-related deaths in men in the U.S.

Diagnosis

The diagnosis of prostate cancer is made by biopsy of the prostate gland. The approach to biopsy has changed over time, especially with the advent of prostate-specific antigen screening programs that identify cancer in prostates that are normal to palpation and to transrectal ultrasound. For patients with an elevated prostate-specific antigen level but with a normal biopsy, questions exist about subsequent evaluation, because repeat biopsy specimens may be positive for cancer in a substantial percentage of patients.

In the early 1990s, use of sextant biopsies involving 6 random, evenly distributed biopsies became the standard approach to diagnose prostate cancer. In the late 1990s, as studies showed high false-negative rates for this strategy (missed cancers), approaches were developed to increase the total number of biopsies and to change the location of the biopsies. While there is disagreement about the optimal strategy, most would agree that initial prostate biopsy strategies should include at least 10 to 14 cores. Additional concerns have been raised about drawing conclusions about the stage (grade) of prostate cancer based on limited biopsy specimens. Use of multiple biopsies has also been discussed as an approach to identify tumors that may be eligible for subtotal cryoablation therapy.

At present, many practitioners use a 12- to 14-core "extended" biopsy strategy for patients undergoing initial biopsy. This extended biopsy is done in an office setting and allows for more extensive sampling of the lateral peripheral zone; a sampling of the lateral horn might increase the cancer detection rate by approximately 25%.[1]

Another approach to increasing the number of biopsy tissue cores is "saturation" biopsy. In general, saturation biopsy is considered as more than 20 cores taken from the prostate, with an improved sampling of the anterior zones of the gland, which may be undersampled in standard peripheral zone biopsy strategies and might lead to missed cancers. Saturation biopsy might be performed transrectally or transperineally; the transperineal approach is generally performed as a stereotactic template-guided procedure with general anesthesia.

Surveillance

In addition to the diagnosis of prostate cancer, some have suggested that saturation biopsy could be a part of active surveillance (a treatment approach that involves surveillance with prostate-specific antigen, digital rectal exam, and routine prostate biopsies in men whose cancers are small and expected to behave indolently). Saturation biopsy has the potential to identify tumor grade more accurately than standard biopsy.

Literature Review

Evidence reviews assess whether a medical test is clinically useful. A useful test provides information to make a clinical management decision that improves the net health outcome. That is, the balance of benefits and harms is better when the test is used to manage the condition than when another test or no test is used to manage the condition.

The first step in assessing a medical test is to formulate the clinical context and purpose of the test. The test must be technically reliable, clinically valid, and clinically useful for that purpose. Evidence reviews assess the evidence on whether a test is clinically valid and clinically useful. Technical reliability is outside the scope of these reviews, and credible information on technical reliability is available from other sources.

Initial or Repeat Saturation Biopsy

Clinical Context and Test Purpose

The proposed clinical utility of saturation biopsy for the diagnosis of prostate cancer is to improve health outcomes by detecting more clinically significant cancers and intervening appropriately. To evaluate the impact of saturation biopsy on the net health outcome, studies are needed that compare rates of clinically significant prostate cancers detected using saturation biopsy versus other biopsy methods.

The following PICO was used to select literature to inform this review. They apply to the first 2 indications: initial or repeat saturation biopsy.

Populations

The relevant population of interest is individuals with suspected prostate cancer.

Interventions

The therapy being considered is an initial or repeat saturation biopsy. Saturation biopsy is generally considered obtaining more than 20 biopsy tissue cores from the prostate in a systematic manner; it is occasionally defined as obtaining more than 18 biopsy tissue cores. Saturation biopsy can be performed transrectally or transperineally; the transperineal approach is generally performed as a stereotactic template-guided procedure with general anesthesia.

Comparators

The following practice is currently being used: standard biopsy.

Outcomes

The general outcomes of interest are test accuracy, overall survival (OS), disease-specific survival, and treatment-related morbidity (Table 1).

Specific outcomes are improving the detection of clinically significant prostate cancer; increasing accurate risk stratification; and reducing the overdiagnosis of indolent tumors requiring only active surveillance. These are outcomes of primary interest because they would inform the individual's treatment plan and consequently, impact health outcomes.

Change in detection rate alone is not sufficient to determine the impact of saturation biopsy on health outcomes compared with other biopsy methods. With higher detection rates, there is the possibility of detecting clinically insignificant cancers, which could lead to unnecessary treatment. False-positive test results can lead to overdiagnosis and overtreatment, which exposes individuals to potential treatment morbidity without benefit. False-negative test results can lead to failure to diagnose clinically significant cancers that require definitive treatment. In addition, studies would ideally evaluate the impact of saturation biopsy on health outcomes such as disease progression or mortality.

Diagnostic accuracy is a short-term outcome. Survival outcomes would be measured over the long-term (e.g., 5- or 10-year survival).

Table 1. Outcomes of Interest for Individuals with Suspicion of Prostate Cancer

Outcomes	Details
Test accuracy	Overall prostate cancer detection, clinically significant prostate cancer detection, sensitivity, and specificity [Timing: ≥1 week]
Health Outcomes	Overall survival, disease-specific survival, treatment-related morbidity [Timing: 5 to 10 years]

Study Selection Criteria

For the evaluation of clinical validity of the saturation biopsy test, studies that meet the following eligibility criteria were considered:

- Reported on the accuracy of the marketed version of the technology (including any algorithms used to calculate scores)
- Included a suitable reference standard
- Patient/sample clinical characteristics were described
- Patient/sample selection criteria were described.

Review of Evidence

Initial Saturation Biopsy

Clinically Valid

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Systematic Reviews

The literature on diagnostic accuracy consists of studies reporting prostate cancer detection rates or diagnostic yields as a primary outcome. These data were summarized in a systematic review by Jiang et al (2013) on the utility of an initial transrectal saturation biopsy compared with an extended biopsy strategy.[2] Eight studies (N=11,997) met eligibility criteria (i.e., compared 2 biopsy strategies on initial biopsy). Two of the studies were randomized controlled trials (RCTs), 1 used a paired design, and 5 were nonrandomized trials. Overall, prostate cancer was diagnosed in 2328 (42.4%) of 5486 men who underwent saturation biopsy compared with 2562 (39.3%) of 6511 men who had an extended biopsy. The detection rate was statistically significantly higher in the saturation biopsy group (risk difference, 0.004; 95% confidence interval [CI], 0.01 to 0.008; p=.002). When only the higher-quality studies were analyzed (i.e., the RCTs and prospective paired design), the detection rate remained statistically significantly higher for saturation biopsy (risk difference, 0.03; 95% CI, 0.01 to 0.05; p=.01). Subgroup analysis found that the difference in detection rates between saturation and extended biopsy strategies was limited to the subgroup of men with prostate-specific antigen (PSA) levels less than 10 ng/mL. Within this group, prostate cancer was diagnosed in 998 (38%) of 2597 men who had saturation biopsies and in 1135 (34%) of 3322 men with extended biopsies (risk difference, 0.04; 95% CI, 0.01 to 0.07; p=.002). Although the subgroup analyses included individual risk factors such as PSA level, they did not differentiate between detection of lower and higher risk prostate cancers. In addition, differences in health outcomes (e.g., progression-free survival, OS) were not reported.

A related meta-analysis was published by Xue et al (2017).[3] Reviewers evaluated the literature comparing transrectal and transperineal biopsy approaches for the detection of prostate cancer. In an analysis stratified by the number of biopsy cores, there was no significant difference in the prostate cancer detection rate with the transrectal strategy or the transperineal biopsy strategy in studies using extended biopsy (odds ratio [OR], 1.14; 95% CI, 0.89 to 1.45) or studies using saturation biopsy (OR, 1.11; 95% CI, 0.92 to 1.34).

Observational Studies

A retrospective nonrandomized study by Li et al (2014) reviewed data on 438 men who received an initial saturation biopsy and 3338 men who had an initial extended prostate biopsy.[4] In an analysis stratified by PSA levels, there was a statistically significant higher rate of prostate cancer detection using a saturation biopsy strategy in men with a PSA level of less than 10 ng/mL. Detection rates

among men with a PSA level of less than 4 ng/mL were 47.1% (40/85) with saturation biopsy and 32.8% (288/878) with extended biopsy (p=.008). Rates among men with PSA levels between 4 ng/mL and 9.9 ng/mL were 50.9% (144/283) with saturation biopsy and 42.9% (867/2022) with extended biopsy (p=.011). There was no statistically significant difference in detection rates between groups when PSA levels were greater than 10 ng/mL. Detection rates at PSA levels greater than 10 ng/mL were 60% (42/70) with saturation biopsy and 61% (267/438) with extended biopsy (p=.879).

A related study by Li et al (2014) evaluated the potential benefit of saturation biopsy as the initial prostate biopsy strategy by examining the yield of repeat saturation biopsy in men with initial negative findings by either saturation or an extended prostate biopsy.[5] A total of 561 men were included in the study; the initial strategy was saturation biopsy in 81 men and extended biopsy in 480 men. In all cases, saturation biopsy was used for the first repeat biopsy. The overall prostate cancer detection rates were 19.8% in the group with initial saturation biopsy and 34.8% in the group with initial extended biopsy (p=.008). Low-risk prostate cancer was defined using the Epstein criteria (i.e., Gleason score ≤6, PSA density ≤0.15 ng/mL per gram, <3 positive cores, and <50% cancer involvement in a single core). The number of intermediate- and/or high-risk prostate cancers (i.e., not low-risk) identified at first repeat biopsy was 4 (4.9%) of 81 in the initial saturation biopsy group and 85 (17.3%) of 490 in the initial extended biopsy group (p=.048). The statistically significantly lower prostate cancer detection rate among men who initially underwent saturation biopsy would suggest that initial saturation biopsy might be less likely to miss prostate cancer than extended biopsy, and, in this study, prostate cancer diagnosed by repeat saturation after negative initial saturation biopsy was more likely to be clinically insignificant. However, the study indirectly evaluated the initial biopsy, and the number of events in men who underwent an initial saturation biopsy was relatively small.

Clinically Useful

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

No direct evidence from studies comparing the impact of saturation biopsy with standard biopsy for patient management decisions or health outcomes in patients with suspected prostate cancer was identified.

Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Because the evidence is insufficient to demonstrate the detection of clinically significant cancers with saturation biopsy, no inferences can be made about clinical utility.

Subsection Summary: Initial Saturation Biopsy

Studies on saturation biopsy as the initial prostate biopsy strategy were summarized in a 2013 systematic review of 8 studies (2 were RCTs). The prostate cancer detection rate was significantly higher in men with saturation biopsy than in men with standard biopsy. In a subgroup analysis, the systematic review found that the higher detection rate was limited to men with PSA levels less than 10 ng/mL. Health outcomes (e.g., survival rate) were not reported. Although several studies were published after the systematic review, none showed that initial saturation biopsy detected more clinically significant cancers and none reported progression or survival outcomes.

Repeat Saturation Biopsy

Clinically Valid

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Systematic Review

Eichler et al (2006) published a systematic review of cancer detection rates and complications of various prostate biopsy strategies.[6] They pooled data that compared various extended biopsy schemes for studies involving 20,698 patients. Reviewers concluded that prostate biopsy schemes consisting of 12 cores that add laterally directed cores to the standard sextant scheme seem to have the right balance between the cancer detection rate and adverse events and that taking more than 12 cores added no significant benefit.

Observational Studies

Representative studies of saturation biopsy in repeat prostate biopsies follow. These studies focused on cancer detection rates and did not report health outcomes (e.g., OS, progression-free survival).

Mabjeesh et al (2012) reported on a high-risk group of men with at least 2 previous negative transrectal biopsies who then underwent transperineal template-guided saturation biopsy.[7] Prostate cancer was detected in 24 (26%) of the 92 patients, predominantly in the anterior zones. A median of 30 cores was taken in the saturation biopsies. Gleason scores of 7 or higher were detected in 11 (46%) of the diagnosed men. Most tumors (83.3%) were found in the anterior zones of the gland, with a significantly higher number of positive cores than in the posterior zones (mean, 4.9 vs. 1.5, p=.015).

Lee et al (2011) evaluated the role of transrectal saturation biopsy for cancer detection in men with high-grade prostatic intraepithelial neoplasia diagnosed by extended biopsy.[8] From 1999 to 2009, 314 men had at least 1 or more repeat biopsies due to the presence of exclusive high-grade prostatic intraepithelial neoplasia (without any other pathologic finding) in a previously extended biopsy. They were divided into 2 groups according to the initial follow-up biopsy scheme; 178 men were followed using a second standard extended biopsy scheme, and 136 were followed using the saturation biopsy scheme. In the standard repeat biopsy group, 35 (19.7%) of 178 men had cancer on initial repeat biopsy. In the saturation biopsy group, 42 (30.9%) of 136 had cancer on initial repeat biopsy (overall, p=.04). Multivariate analysis demonstrated that the biopsy scheme on repeat biopsy was an independent predictor of prostate cancer detection (OR, 1.85; 95% CI, 1.03 to 3.29), exclusive of age, PSA level, days from initial biopsy, digital rectal exam status, and multifocal prostatic epithelial neoplasia. Pathologic findings on repeat biopsies demonstrated similar Gleason scores, regardless of biopsy technique: a Gleason score of 6 was present in 74.3% and 73.1% of specimens in the standard and saturation schemes, respectively. The presence of a Gleason score of 8 or higher was 8.6% and 9.5%, respectively.

Zaytoun et al (2011) reported on the results of a prospective, nonrandomized comparative study of extended biopsy versus office-based transrectal saturation biopsy in a repeat biopsy population.[9] After an initial negative biopsy, 1056 men underwent a repeat 12- to 14-core biopsy (n=393) or a 20- to 24-core repeat biopsy (n=663) at the discretion of the attending urologist's practice pattern. Indications for the second biopsy included a previous suspicious pathologic finding and/or clinical indications such as an abnormal digital rectal exam, persistently increased PSA level, and PSA level increasing more than 0.75 ng/mL annually. Prostate cancer was detected in 29.8% (n=315) of repeat biopsies. The saturation biopsy group had a detection rate of 32.7% versus 24.9% in the extended biopsy group (p=.008). Of the 315 positive biopsies, 119 (37.8%) revealed clinically insignificant cancer (defined as Gleason score <7, a total of ≤3 positive cores, and maximum of ≤50% of cancer in any positive core). There was a trend toward increased clinically insignificant cancer detection for saturation biopsy (40.1%) versus extended biopsy (32.6%; p=.02).

Clinically Useful

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

No direct evidence from studies comparing the impact of saturation biopsy with standard biopsy for patient management decisions or health outcomes in patients requiring a repeat biopsy for suspected prostate cancer was identified.

Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Because the evidence is insufficient to demonstrate the detection of clinically significant cancers with saturation biopsy, no inferences can be made about clinical utility.

Subsection Summary: Repeat Saturation Biopsy

Several studies have compared saturation with standard prostate biopsies in the repeat biopsy setting and have found significantly higher detection rates with saturation biopsy. However, at least 1 study found that about one-third of the positive findings with saturation biopsy were clinically insignificant cancers. Moreover, studies of saturation biopsy as the repeat prostate biopsy strategy focused on cancer detection rates and did not report health outcomes (e.g., progression or survival).

Active Surveillance

Clinical Context and Test Purpose

The proposed clinical utility of saturation biopsy is to improve health outcomes by better identifying individuals with prostate cancer who are appropriate candidates for active surveillance through more accurate determination of the Gleason score.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with prostate cancer who are potential candidates for active surveillance.

Interventions

The test being considered is a saturation biopsy. Saturation biopsy is generally considered obtaining more than 20 biopsy tissue cores from the prostate in a systematic manner; it is occasionally defined as obtaining more than 18 biopsy tissue cores. Saturation biopsy can be performed transrectally or transperineally; the transperineal approach is generally performed as a stereotactic template-guided procedure with general anesthesia.

Comparators

The following practice is currently being used: standard biopsy.

Outcomes

The general outcomes of interest are test accuracy, OS , disease-specific survival, and treatment-related morbidity.

The Gleason score is a criterion used to select men for active surveillance. More accurate selection of individuals for active surveillance could lead to better health outcomes by reducing misclassification of individuals as being sufficiently low-risk that active surveillance is an appropriate approach to individual management.

Diagnostic accuracy is a short-term outcome. Survival outcomes would be measured over the long-term (e.g., 5- or 10-year survival).

Study Selection Criteria

For the evaluation of clinical validity of the saturation biopsy test, studies that meet the following eligibility criteria were considered:

- Reported on the accuracy of the marketed version of the technology (including any algorithms used to calculate scores)
- Included a suitable reference standard
- Patient/sample clinical characteristics were described
- Patient/sample selection criteria were described.

Review of Evidence

Clinically Valid

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Observational Studies

Several studies have evaluated the accuracy of saturation biopsy for identifying patients who might be suitable candidates for active surveillance. Linder et al (2013) reviewed data on 500 consecutive patients who underwent standard template prostate biopsy (12 cores) or saturation biopsy (at least 18 cores) before radical prostatectomy.[10] They identified 218 patients who would have been candidates for active surveillance. Criteria were a Gleason score no greater than 6, clinical stage T1 or T2a, PSA level less than 10 ng/mL, and involvement of no more than 33% of cores. Among these 218 patients, 124 had undergone standard biopsy and 94 underwent saturation biopsy. In a multivariate analysis, biopsy method was not a significant predictor of upstaging on analysis of pathologic findings (p=.26). In addition, the 5-year biochemical failure-free survival rates (defined as PSA level of at least 0.4 ng/mL) did not differ significantly between groups: rates were 97% for standard biopsy and 95% for saturation biopsy (p=.11).

Quintana et al (2016) compared 12-core biopsy with saturation biopsy (18 to 33 cores; median, 20 cores) in 375 patients to determine the Gleason score accurately.[11] The authors stated that patients with Gleason scores of 4 or higher were generally not considered candidates for active surveillance. Gleason score was confirmed by pathologic analysis of prostate specimens. For detecting a high Gleason grade (i.e., ≥4), there were no statistically significant differences in the sensitivity, specificity, negative predictive value, or positive predictive value of 12-core versus saturation biopsies. The areas under the receiver operating characteristic curve were 0.82 for saturation biopsy and 0.84 for 12-core biopsy (p-value not reported).

Clinically Useful

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

No direct evidence from studies comparing the impact of saturation biopsy with standard biopsy for patient management decisions or health outcomes in patients with prostate cancer being considered for active surveillance was identified.

Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Because the evidence is insufficient to demonstrate that saturation biopsy improves the identification of tumor grade, no inferences can be made about clinical utility.

Section Summary: Active Surveillance

Several studies have compared saturation with standard prostate biopsies in the active surveillance setting and have failed to find differences between these methods. In 1 study, biopsy method was not a significant predictor of upstaging and, in the other study, biopsy method was not significantly associated with selecting patients with a high Gleason score.

Supplemental Information

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

2014 Input

In response to requests, input was received from 3 physician specialty societies and 3 academic medical centers while this policy was under review in 2014. There were 5 responses from 1 specialty society, 4 responses from another, and 1 response from the third, for a total of 10 specialty society responses. Most reviewers stated that saturation biopsy is considered investigational and did not think that saturation biopsy in patients with 2 prior negative biopsies and persistently rising prostate-specific antigen level is considered medically necessary. Clinicians proposed various options that could be used in the situation of prior negative biopsies and rising prostate-specific antigen level: there was no consensus on the best approach. Suggestions included magnetic resonance imaging with transrectal ultrasound, multiparametric magnetic resonance imaging, and 3T pelvic magnetic resonance imaging. There was near consensus that there is insufficient evidence to support the use of any of these techniques for the indications being considered.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a U.S. professional society, an international society with U.S. representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

National Comprehensive Cancer Network Guidelines

The National Comprehensive Cancer Network (NCCN) guidelines on early detection of prostate cancer (v.1.2025) state that despite emerging evidence, the panel does not recommend a saturation biopsy strategy for all individuals with previous negative biopsies given the benefits seen for magnetic resonance imaging (MRI) and MRI-targeted biopsy in this patient population.[12] The emerging evidence cited included 1 prospective nonrandomized study (Zaytoun et al 2011)[9] and uncontrolled observational studies published between 2006 and 2013.

NCCN guidelines on prostate cancer treatment (v.2.2025) do not mention saturation biopsy.[13]

U.S. Preventive Services Task Force Recommendations

The U.S. Preventive Services Task Force (2018) recommendations on prostate cancer screening did not address saturation biopsy.[14] This topic is currently being updated.

Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials

A search of ClinicalTrials.gov in May 2025 did not identify any ongoing or unpublished trials that would likely influence this review.

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12. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Prostate Cancer Early Detection. Version 1.2025 https://www.nccn.org/professionals/physician_gls/pdf/prostate_detection.pdf. Accessed May 14, 2025.
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14. U.S. Preventive Services Task Force (USPSTF). Final Recommendation Statement: Prostate Cancer: Screening. 2018 May;

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Documentation for Clinical Review

Please provide the following documentation:

- History and physical and/or consultation notes including:
  - Prior treatments and response
  - PSA lab results
  - All pertinent lab results
  - All imaging results/reports

Post Service (in addition to the above, please include the following):

- Operative/procedure report(s)

Coding

The list of codes in this Medical Policy is intended as a general reference and may not cover all codes. Inclusion or exclusion of a code(s) does not constitute or imply member coverage or provider reimbursement policy.

Type	Code	Description
CPT®	55700	Biopsy, prostate; needle or punch, single or multiple, any approach
	55706	Biopsies, prostate, needle, transperineal, stereotactic template guided saturation sampling, including imaging guidance
	76942	Ultrasonic guidance for needle placement (e.g., biopsy, aspiration, injection, localization device), imaging supervision and interpretation
HCPCS	G0416	Surgical pathology, gross and microscopic examinations, for prostate needle biopsy, any method

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action
12/01/2025	New policy.

Definitions of Decision Determinations

Healthcare Services: For the purpose of this Medical Policy, Healthcare Services means procedures, treatments, supplies, devices, and equipment.

Medically Necessary or **Medical Necessity** means reasonable and necessary services to protect life, to prevent significant illness or significant disability, or alleviate severe pain through the diagnosis or treatment of disease, illness, or injury, as required under W&I section 14059.5(a) and 22 CCR section 51303(a). Medically Necessary services must include services necessary to achieve age-appropriate growth and development, and attain, maintain, or regain functional capacity.

For Members less than 21 years of age, a service is Medically Necessary if it meets the Early and Periodic Screening, Diagnostic, and Treatment (EPSDT) standard of Medical Necessity set forth in 42

USC section 1396d(r)(5), as required by W&I sections 14059.5(b) and 14132(v). Without limitation, Medically Necessary services for Members less than 21 years of age include all services necessary to achieve or maintain age-appropriate growth and development, attain, regain or maintain functional capacity, or improve, support, or maintain the Member's current health condition. Contractor must determine Medical Necessity on a case-by-case basis, taking into account the individual needs of the Child.

Criteria Determining Experimental/Investigational Status

In making a determination that any procedure, treatment, therapy, drug, biological product, facility, equipment, device, or supply is "experimental or investigational" by the Plan, the Plan shall refer to evidence from the national medical community, which may include one or more of the following sources:

1. Evidence from national medical organizations, such as the National Centers of Health Service Research.
2. Peer-reviewed medical and scientific literature.
3. Publications from organizations, such as the American Medical Association (AMA).
4. Professionals, specialists, and experts.
5. Written protocols and consent forms used by the proposed treating facility or other facility administering substantially the same drug, device, or medical treatment.
6. An expert physician panel selected by one of two organizations, the Managed Care Ombudsman Program of the Medical Care Management Corporation or the Department of Managed Health Care.

Feedback

Blue Shield of California Promise Health Plan is interested in receiving feedback relative to developing, adopting, and reviewing criteria for medical policy. Any licensed practitioner who is contracted with Blue Shield of California Promise Health Plan is welcome to provide comments, suggestions, or concerns. Our internal policy committees will receive and take your comments into consideration. Our medical policies are available to view or download at www.blueshieldca.com/en/bsp/providers.

For medical policy feedback, please send comments to: MedPolicy@blueshieldca.com

Questions regarding the applicability of this policy should be directed to the Blue Shield of California Promise Health Plan Prior Authorization Department at (800) 468-9935, or the Complex Case Management Department at (855) 699-5557 (TTY 711) for San Diego County and (800) 605-2556 (TTY 711) for Los Angeles County or visit the provider portal at www.blueshieldca.com/en/bsp/providers.

Disclaimer: Blue Shield of California Promise Health Plan may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as member health services contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member health services contracts may differ in their benefits. Blue Shield of California Promise Health Plan reserves the right to review and update policies as appropriate.