



**Clinical Review Criteria  
Radioimmunosciintigraphy**

- ProstaScint (Indium In 111 Capromab Pendetide, Capromab)

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**Criteria**

**For Medicare Members**

Source	Policy
CMS Coverage Manuals	None
National Coverage Determinations (NCD)	None
Local Coverage Determinations (LCD)	None
Local Coverage Article	None
Kaiser Permanente Medical Policy	Due to the absence of an active NCD, LCD, or other coverage guidance, Kaiser Permanente has chosen to use their own Clinical Review Criteria, "Radioimmunosciintigraphy" for medical necessity determinations. Refer to the Non-Medicare criteria below.

**For Non-Medicare Members**

There is insufficient evidence in the published medical literature to show that this service/therapy is as safe as standard services/therapies and/or provides better long-term outcomes than current standard services/therapies.

The following information was used in the development of this document and is provided as background only. It is provided for historical purposes and does not necessarily reflect the most current published literature. When significant new articles are published that impact treatment option, Kaiser Permanente will review as needed. This information is not to be used as coverage criteria. Please only refer to the criteria listed above for coverage determinations.

**Background**

Prostate cancer is the most frequently diagnosed malignancy in the US, and second leading cause of death in men. In the era of prostate specific antigen (PSA) testing, prostate cancer is detected at an earlier stage, and about 85% of newly diagnosed patients have a localized disease that may be treated with definitive radical prostatectomy or radiation therapy. Though these are considered definitive treatments, 15-40% of the patients will develop biochemical PSA relapse within 10 years. The disease may recur locally in the prostatic fossa, in the regional lymph nodes, or at distant sites (Nagda 2007, Raj 2001, Pukar 2008).

The appropriate management of prostate cancer is highly dependent on accurate information about the location and extent of the disease. Surgical resection of the prostate is not indicated for patients whose disease has spread outside the prostatic bed. Although a rising PSA level may be indicative of prostate cancer and a residual or recurrent disease after radical prostatectomy, it is not specific and cannot determine the stage of the disease or discriminate between local cancer and metastatic involvement. Normograms, or clinical algorithms (e.g. that developed by Partin and colleagues in the early 1990s), use a combination of serum PSA level, Gleason score, and clinical stage to predict the likelihood of extraprostatic disease in order to help with treatment decisions. The normograms offer a statistical probability of disease organ confinement for populations of patients with similar clinical variables, but sometimes do not apply to the individual patient, who may need to be evaluated further. Traditionally patients undergo transrectal ultrasound with biopsy to assess local tumor, chest x-ray to look for any

lung metastases, bone scan to determine the presence of osseous metastases, and CT scan or MRI of the abdomen, and pelvis to evaluate lymph node for disease involvement. After definitive treatment of the cancer, patients are followed up with periodic measurement of PSA levels and digital rectal examination (DRE). Imaging is performed if there are suspicious findings on DRE, PSA relapse, or if the patients have symptoms such as bone pain. Distinguishing between local versus systemic extent of the disease in patients with a PSA relapse is crucial for determining the salvage treatment modality. Salvage radiation therapy is used for local recurrence in the prostatic fossa, and systemic therapy is considered for those with a disease outside the fossa.

Conventional CT scans and MRI may be helpful in evaluating patients who have advanced disease with adjacent organ invasion and distant lymph adenopathy but have limited clinical value in local staging or detecting early recurrence of the tumor. CT and MRI classify metastatic nodes strictly by size; they are classified as normal if they are one centimeter or less in diameter, and as abnormal if larger. The majority of patients presenting with clinically localized prostate carcinoma and occult lymph node metastases have either microscopic involvement or a disease volume less than 1 cm<sup>3</sup>, which would go undetected. On the other hand, inflammatory or hyperplastic nodes greater than one centimeter in diameter might be erroneously classified as neoplastic (Polascik 1999, Raj 2002, Bander 2006, Nagda 2007).

In contrast to anatomic imaging, radioimmunoscintigraphy is a functional imaging modality which acquires images through the use of a radiolabeled antibody that selectively recognizes malignant tissue. One antigen of interest for prostate cancer is prostate-specific epithelial cell membrane antigen (PSMA) which is expressed at high levels in prostate cancers. The expression increases as the tumor grade increases, and in metastatic deposits. It increases further as the tumor becomes androgen independent.

Capromab pendetide (ProstaScint) is a murine monoclonal antibody that reacts with PSMA. Immunoscintigraphy is accomplished by labeling the antibody with indium 111. After infusion of the antibody, whole body planar and single-photon emission CT images are obtained. ProstaScint images can potentially aid in patient management by helping identify when the cancer has spread outside the prostatic bed to regional lymph nodes or to distant soft tissue sites. Capromab however, recognizes a molecular site that is masked in viable cells, and detects antigenic sites on the intracellular portion of PSMA, a site not accessible to circulating antibody. It thus cannot adequately image bone metastases, which are the most common and earliest site of metastatic spread in prostate cancer (Haseman 2007, Akin 2007).

Indium-capromab pendetide (ProstaScint, Cytogen, Princeton, NJ) was approved by the FDA in 1996 as an immunoscintigraphic diagnostic imaging agent for newly diagnosed patients with biopsy-proven prostate cancer, who are at high risk for pelvic lymph node metastases, and in patients with a rising PSA levels after prostatectomy.

## Medical Technology Assessment Committee (MTAC)

### *Radioimmunoscintigraphy for the Diagnosis of Prostate Cancer*

#### **06/12/2009: MTAC REVIEW**

**Evidence Conclusion:** As indicated earlier, 111Indium capromab pendetide (ProstaScint) scan was studied in two clinical settings. 1. Presurgical staging of prostate cancer, and 2. Post prostatectomy biochemical failure. Presurgical staging of prostate cancer: Polascik and colleagues (1999) compared the accuracy and predictive values of ProstaScint with various algorithms/normograms used to predict lymph node involvement prior to surgery, and Manyak and colleagues (1999) compared it with CT scan and MRI results. The gold standard was pathological results of surgically resected lymph nodes. Bone metastases were not evaluated. These, as well as other published studies, included patients at high risk of extraprostatic disease. The overall results show that ProstaScint had sensitivity around 62%, specificity ranging from 72-80%, and a positive predictive value ranging from 62-66% in detecting lymph node involvement. The observed ProstaScint sensitivity in predicting lymph node metastases was higher than CT and MRI but lower than the various clinical algorithms based on a PSA level, biopsy Gleason score, and clinical stage. The predictive value of Partin's normogram was not improved when combined with ProstaScint scan. There are no published follow-up studies to indicate that high-risk patients with a negative capromab pendetide scan have a lower failure rate after surgery. Biochemical failure after prostatectomy: There were no randomized controlled trials that compared outcomes of salvage radiation therapy in patients with and without ProstaScint imaging. The published studies retrospectively examined the association of negative and positive ProstaScint scans on PSA regression and/ or survival after salvage radiotherapy to the prostate fossa. The studies had their limitations, potential biases and confounding, and had conflicting results. Nagda and colleagues (2007), Wilkinson and Chodak (2004), and Thomas et al (2003) study results all indicated that ProstaScint scans has limited value in making clinical decisions.

Nagda et al's study showed no significant difference in relapse free survival between patients who showed or did not show a positive capromab pendetide uptake. Wilkinson and Chodak 2004, found that less than half of the patients with a localized uptake of ProstaScint scan had a durable response after salvage radiation therapy. Thomas and colleagues 2003 found no statistically significant association between ProstaScint scan findings and the response to salvage radiotherapy. On the other hand, other the results of other studies (Haseman 2007, Proano 2006, Kahn 1998, and Levesque 1998) suggested that ProstaScint scan might be useful in selecting patients for salvage radiotherapy therapy. Haseman et al study (2007) showed that overall death, and prostate cancer specific death rates were significantly higher among patients with central abdominal ProstaScint uptake. Praono and colleagues 2006, found that patients with negative ProstaScint scans had significantly lower PSA progression rate after salvage radiotherapy than those with a positive scan. They however indicated that the finding might be dependent on the pre-radiotherapy PSA level. Kahn et al 1998, and Levesque and colleagues 1998, also suggested that ProstaScint scan might be useful in selecting patients for salvage radiotherapy therapy. RCTs comparing salvage radiation therapy in patients with and without ProstaScint imaging would help determine the role of the scan in predicting success of salvage radiation therapy after failed definitive treatment. **Conclusion:** There is insufficient evidence to determine that ProstaScint would improve presurgical staging of prostate cancer, differentiate between local and distant spread in patients with biochemical failure after definitive treatment, or predict success of salvage radiation therapy.

**Articles:** The literature search revealed around 110 articles on Capromab pendetide (ProstaScint). The published studies examined the utility of ProstaScint/ radioimmunoscintigraphy in two settings: 1. Presurgical staging 2. PSA biochemical failure after prostatectomy. Presurgical staging: There were five studies that used surgical pathology results of resected lymph nodes as a gold standard. The three larger studies (N=195, N=152, and N= 51) were conducted by the same study group and most probably with overlapping populations. The other two were very small (N=19, and N=22). The study with the largest population size, as well as the study that compared the accuracy of ProstaScint vs. CT and MRI were selected for critical appraisal. PSA biochemical failure after prostatectomy: The utility of radioimmunoscintigraphy in patients with biochemical failure after definitive therapy was examined for: Its ability to differentiate between local and distant recurrence of the disease: There were 2 retrospective case series with no comparison group, and a very small study that compared the detection of metastatic disease by capromab vs. CT which have limited utility for detecting early recurrence of the disease. The search also revealed a small study on the impact of fusion of capromab pendetide data with those from MRI or CT in patients with recurrent prostate cancer. Due to the small size, design and quality of the studies, none was selected for critical appraisal. Its ability to predict response to salvage therapy: The literature search did not reveal any randomized controlled trials comparing outcome of salvage radiation therapy in patients with and without ProstaScint. There were seven retrospective studies; four examined the association between ProstaScint and PSA progression rate in patients after salvage radiotherapy, and three with survival/mortality outcomes. Two studies with mortality outcomes and one on PSA progression were selected for critical appraisal, based on methodology, size, and duration of follow-up. The following studies were critically appraised: Haseman MK, Rosenthal SA, Kipper SL, et al. Central abdominal uptake of indium-111 capromab pendetide (ProstaScint) predicts for poor prognosis in patients with prostate cancer. *Urology* 2007;70:303-308 See [Evidence Table](#). Manyak MJ, Hinkle GH, Olsen JO, et al. Immunoscintigraphy with indium-111-capromab pendetide: evaluation before definitive therapy in patients with prostate cancer. *Urology* 1999;54:1058-1063 See [Evidence Table](#). Nagda SN, Mohideen N, Lo SS, et al. Long-term follow-up of 111In-capromab pendetide (ProstaScint) scan as pretreatment assessment in patients who undergo salvage radiotherapy for rising prostate-specific antigen after radical prostatectomy for prostate cancer. *Int J Radiation Oncol Biol Phys* 2007; 67:834-840. See [Evidence Table](#). Polascik TJ, Manyak MJ, Haseman MK, et al, Comparison of clinical staging algorithms and 111indium-capromab pendetide immunoscintigraphy in the prediction of lymph node involvement in high risk prostate carcinoma patients. *Cancer* 1999;85:1586-92 See [Evidence Table](#). Proano JM, Sodee B, Resnik MI, et al. The impact of a negative (111) indium-capromab pendetide scan before salvage radiotherapy *J of Urol*.2006;175: 1668-1672. See [Evidence Table](#).

The use of Radioimmunoscintigraphy for the diagnosis of prostate cancer does not meet the *Kaiser Permanente Medical Technology Assessment Criteria*.

## Applicable Codes

### Considered Not Medically Necessary

CPT® or HCPC Codes	Description

<b>78800</b>	Radiopharmaceutical localization of tumor, inflammatory process or distribution of radiopharmaceutical agent(s) (includes vascular flow and blood pool imaging, when performed); planar, single area (eg, head, neck, chest, pelvis), single day imaging
<b>With diagnosis codes</b>	
<b>C61</b>	Malignant neoplasm of prostate
<b>C77.2</b>	Secondary and unspecified malignant neoplasm of intra-abdominal lymph nodes
<b>C77.4</b>	Secondary and unspecified malignant neoplasm of inguinal and lower limb lymph nodes
<b>C77.8</b>	Secondary and unspecified malignant neoplasm of lymph nodes of multiple regions
<b>C77.9</b>	Secondary and unspecified malignant neoplasm of lymph node, unspecified
<b>C79.51</b>	Secondary malignant neoplasm of bone
<b>C79.52</b>	Secondary malignant neoplasm of bone marrow
<b>D07.5</b>	Carcinoma in situ of prostate
<b>Z12.5</b>	Encounter for screening for malignant neoplasm of prostate
<b>Z80.42</b>	Family history of malignant neoplasm of prostate
<b>Z85.46</b>	Personal history of malignant neoplasm of prostate
<b>Z90.721</b>	Acquired absence of ovaries, unilateral
<b>Z90.722</b>	Acquired absence of ovaries, bilateral
<b>Z90.79</b>	Acquired absence of other genital organ(s)

**\*Note:** Codes may not be all-inclusive. Deleted codes and codes not in effect at the time of service may not be covered.

\*\*To verify authorization requirements for a specific code by plan type, please use the [Pre-authorization Code Check](#).

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07/15/2009	04/04/2011 <sup>MDCRPC</sup> , 02/07/2012 <sup>MDCRPC</sup> , 12/04/2012 <sup>MDCRPC</sup> , 10/01/2013 <sup>MPC</sup> , 08/05/2014 <sup>MPC</sup> , 06/02/2015 <sup>MPC</sup> , 05/03/2016 <sup>MPC</sup> , 03/07/2017 <sup>MPC</sup> , 01/09/2018 <sup>MPC</sup> , 12/04/2018 <sup>MPC</sup> , 12/03/2019 <sup>MPC</sup> , 12/01/2020 <sup>MPC</sup> , 12/07/2021 <sup>MPC</sup> , 12/06/2022 <sup>MPC</sup>	07/15/2009

<sup>MDCRPC</sup> Medical Director Clinical Review and Policy Committee  
<sup>MPC</sup> Medical Policy Committee

Revision History	Description