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Commissioning policy

Prostate-Specific Membrane Antigen (PSMA) radiotracers in Positron Emission Tomography – Computed Tomography (PETCT) Imaging for individuals with high-risk primary or recurrent prostate cancer (adults) [2307]

Summary

PSMA PET-CT is recommended to be available as a routine commissioning imaging option for adults with high-risk primary or recurrent prostate cancer within the criteria set out in this document. For the purposes of this document, PSMA PETCT refers to PET-CT imaging using either Ga^{68}-PSMA or F^{18}-PSMA radiotracers.

Committee discussion

Clinical Panel agreed with the policy and recommended this proceeds as a routine commissioning policy. Please see Clinical Panel reports for full details of Clinical Panel's discussion.

The Clinical Priorities Advisory Group committee papers can be accessed here: www.england.nhs.uk/publication/prostate-specific-membrane-antigen-radiotracers-in-positron-emission-tomography/

What we have decided

NHS England has carefully considered evidence from two three-paper summaries, expert views, current provision, and the need for a substantive policy position regarding provision of radiotracers for PET-CT imaging for individuals with high-risk primary or recurrent prostate cancer.

We have concluded that there is sufficient evidence to support the commissioning of Prostate-Specific Membrane Antigen (PSMA) radiotracers for PET-CT in adult patients with recurrent prostate cancer and in highly selected patients with high-risk primary prostate cancer where conventional imaging leaves clinically important uncertainties.

Links and updates to other policies and documents

Please refer to Appendix A for all related NICE Technology Appraisal Guidance, clinical policies, and service specifications.

Plain language summary

The condition

The prostate is a small gland located at the base of the bladder. Prostate cancer only affects men[1]; this means that this policy applies to any person with a prostate. Prostate cancer is the most common type of cancer in men and the second most common type of cancer in the UK. This commissioning policy concerns two distinct subgroups of patients with prostate cancer: those with high-risk primary disease suitable for radical, curative treatment and those with biochemical recurrence suitable for salvage therapy.

High-Risk Primary Disease

High-risk primary disease includes individuals who present with clinical and biochemical risk factors which increase the severity of disease. This includes a high prostate specific antigen (PSA) level or high tumour grade. High-risk primary disease refers to disease that has not yet metastasised.

This risk stratification provides guidance on treatment options for each individual patient, which may include radical prostatectomy, radical radiotherapy, hormone therapy or chemotherapy. Treatment options will differ depending on presence of metastases and risk stratification.

Recurrent Disease (biochemical recurrence)

Following radical treatment (radical prostatectomy, radiotherapy, or focal therapy) of prostate cancer, some men will have biochemical recurrence of the cancer. The definition of biochemical recurrence depends on the primary treatment received:

- After radical prostatectomy, biochemical recurrence is defined as a prostate specific antigen (PSA) level over a threshold of 0.2ng/ml (Mottet et al. 2015).
- After radiation therapy, biochemical recurrence is defined as an absolute increase in PSA level of 2ng/ml above the lowest point after treatment.

It is estimated that 20-40% of patients undergoing radical prostatectomy and 30-50% of patients undergoing radiotherapy will experience biochemical recurrence within 10 years (Paller et al, 2013). After biochemical recurrence is detected, the patient could either have salvage treatment with curative intent (external beam radiation therapy to the prostate bed and/or hormone therapy or salvage prostatectomy) or non-curative treatment, depending on fitness and co-morbidities.

About PET-CT Imaging in prostate cancer

Positron Emission Tomography (PET) – Computerised Tomography (CT) is a unique imaging tool which shows pathology by using PET to detect abnormal tissue metabolism and CT to show structural changes. PET-CT uses small amounts of radioactive materials called radiotracers. The radiotracers collect within tissues and help identify abnormal metabolic activity, allowing early and precise identification of disease spread.

PET-CT is commissioned for use along the prostate cancer pathway, specifically to support cancer staging, and to assess whether the cancer has returned (recurrence). Under certain criteria, PET-CT is more specific and sensitive in identifying early metastatic disease than

[1] In this policy the term ‘men’ is used, based on the source evidence used in its development. This policy is also relevant to people with male anatomy who do not identify as men.

conventional imaging[2]. Early identification of metastatic foci with PET-CT enables optimal treatment decisions to be made and can alter the planned treatment choice.

About alternative imaging

Single Photon Emission Computed Tomography-CT (SPECT-CT) with a technetium radiotracer is an alternative imaging option when PET-CT is not available.

About prostate specific radiotracers

In accordance with NHS England's published clinical commissioning policy statement for PET-CT, only choline derived radiotracers are currently routinely commissioned for use in prostate cancer scanning. Choline metabolism is altered in prostate cancer cells. As tumour cells present a high metabolic rate, radiolabelled choline uptake increases in tumour tissue, allowing diagnosis and staging of individuals. Radiolabelled choline is an unlicensed product.

The commissioning criteria for the use of choline PET-CT is as follows:

- Evaluation of equivocal findings on conventional imaging such as possible nodal or metastatic disease in patients with prostate cancer where confirmation or exclusion of distant disease would directly influence patient management; and
- Suspected recurrence in patients with a rapidly rising PSA or indeterminate or equivocal conventional imaging where the results would directly influence patient management.

This commissioning policy sets out the eligibility criteria for PSMA PET-CT radiotracers commissioned by NHS England for patients with high-risk primary prostate cancer or biochemical recurrence. This commissioning policy will supersede the current interim commissioning position for reimbursement of PSMA radiotracers. Commissioned providers may use Ga^{68}-PSMA, F^{18}-PSMA or choline radiotracers for PETCT depending on availability and supply.

PSMA radiotracers work by targeting the PSMA protein which is only expressed by prostate cancer cells. PSMA is overexpressed in 95% of prostate cancer cells but the overexpression of PSMA has not been found in benign prostatic diseases such as prostatic hyperplasia. Although the target is the same, both Ga^{68}-PSMA and F^{18}-PSMA have slightly different imaging characteristics. Both Ga^{68}-PSMA and F^{18}-PSMA are unlicensed products.

The eligibility criteria for choline-based PET-CT imaging is set out in the PET-CT clinical commissioning policy statement: Positron Emission Tomography - Computed Tomography (PET-CT) Guidelines (all ages).

Epidemiology and needs assessment

There are around 52,300 new cases of prostate cancer in the UK each year (Cancer Research UK). Approximately 15% of patients are diagnosed with high-risk disease at presentation. Most of these will likely not require PSMA PET-CT. Assuming only 10% have equivocal lesions on conventional imaging, this would equate to 665 high-risk patients per year.

It is estimated that approximately 12,000 patients present with biochemical recurrence each year in the UK and, of these, approximately 8,000 patients are eligible for PET-CT.

[2] Conventional imaging refers to a CT scan of the chest, abdomen and pelvis and a bone scan.

Adding all the different indications for PSMA PET-CT gives a total per year of 8,665. However, given that the estimates above are likely to be higher than actual figures, it is felt an estimate of 8,000 per year is more likely to be correct. This also correlates with previous figures for PET-CT for prostate cancer.

Evidence summary

Two independent three paper summaries were conducted for the use of PSMA PET-CT in prostate cancer. NHS England has concluded that there is sufficient evidence to support a policy for the routine commissioning of PSMA PET-CT for high-risk primary and biochemical recurrence of prostate cancer.

The three paper summaries which inform this commissioning position can be accessed here: www.england.nhs.uk/publication/prostate-specific-membrane-antigen-radiotracers-in-positron-emission-tomography/

Implementation

Inclusion Criteria

Patients aged 18 years or over are eligible for PSMA PET-CT scanning if they meet the either of the following clinical indications:

1. Staging in high-risk[3] primary prostate cancer

- Patients with high-risk primary disease with equivocal lesions on baseline conventional staging imaging where confirmation or exclusion of distant disease would directly influence patient management. High-risk primary disease is determined by ANY of the following:
    - Elevated prostate-specific antigen (PSA) level >20 ng/mL
    - Stage T3 or greater
    - Gleason score ≥8

2. Detection of biochemical recurrence localisation

- Patients who have biochemical recurrence/persistence post radical prostatectomy as defined as a PSA value of greater than or equal to 0.2ng/ml[4] who are suitable for salvage therapy

OR

- Patients who have biochemical recurrence following radical radiotherapy/brachytherapy as defined as a PSA increase greater than or equal to 2ng/ml higher than the nadir PSA value who are suitable for salvage local therapy

Exclusion Criteria

Patients who are unable to undergo radical or salvage treatment due to:

- existing comorbidities preventing them from having further salvage therapy options
- patient choice

[3] High-risk primary prostate cancer can also be defined by Cambridge Prognostic Group (CPG) 4 or 5.

[4] PSMA PET-CET is recommended if the PSA ≥ 0.2ng/ml. Radiolabelled choline is considered a suitable alternative PET tracer where PSMA is unavailable, when PSA levels ≥ 1.0ng/ml.

Governance arrangements

Provider organisations must register all patients using prior approval software and ensure monitoring arrangements are in place to demonstrate compliance against the criteria as outlined.

This document relates to the Positron Emission Tomography – Computed Tomography (PET CT) service specification: Positron Emission Tomography – Computed Tomography (PET CT) Scanning (All Ages).

Mechanism for funding

PSMA PET-CT for prostate cancer will be commissioned and funded by NHS England Specialised Commissioning under existing arrangements for the provision of Specialised Cancer and Radiotherapy services.

Audit requirements

Please refer to the PET-CT 2013 Service Specification for audit requirements.

Policy review date

This document will be reviewed when there are significant changes in clinical evidence which indicates that the policy requires revision. If a review is needed due to a new evidence base then a new Preliminary Policy Proposal needs to be submitted by contacting england.CET@nhs.net.

Equality statement

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and
- Given regard to the need to reduce inequalities between patients in access to, and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities.

Definitions

Positron Emission Tomography – Computed Tomography (PETCT)	PET-CT is an imaging technique which utilises a PET scanner and a CT scanner to acquire a single superposed image.
Radiotracer	Radiotracers are molecules linked to small amounts of radioactive material that light up on medical imaging. Different radiotracers are taken up by different cells. A radiotracer is injected, swallowed, or inhaled and then eventually accumulates in the area of the body under examination.

PSMA	Prostate specific membrane antigen is a molecule that is present on the surface of prostate cancer cells.
PSA	Prostate specific antigen is a protein produced by normal prostate glands. The PSA level can be measured by a blood test. A small amount of PSA in the blood is normal. If the prostate becomes enlarged, inflamed, or infected, larger amounts of PSA get into the blood. The amount of PSA in the blood may also increase if there is cancer in the prostate.

References

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Appendix A

This commissioning policy relates to the following:

Service Specifications

- NHS England Commissioning Service Specification: Positron Emission Tomography – Computed Tomography (PET CT) Scanning (All Ages)

NHS England Clinical Commissioning Policies

- Brachytherapy dose escalation with external beam radiotherapy for intermediate- and high-risk localised prostate cancer
- External beam radiotherapy for patients presenting with hormone sensitive, low volume metastatic prostate cancer at the time of diagnosis
- External beam radiotherapy for patients presenting with hormone sensitive, low volume metastatic prostate cancer at the time of diagnosis
- Robotic assisted surgical procedures for prostate cancer

NHS England Commissioning Policy Statements

- Positron Emission Tomography- Computed Tomography (PET-CT) Guidelines (all ages)
- Docetaxel in combination with androgen deprivation therapy for the treatment of hormone naïve metastatic prostate cancer

Not Routinely Commissioned Clinical Policies

- Proton beam therapy for cancer of the prostate
- Stereotactic ablative radiotherapy in the treatment of prostate cancer

NICE Technology Appraisals

- Enzalutamide for treating hormone-sensitive metastatic prostate cancer (TA712)
- Degarelix for treating advanced hormone-dependent prostate cancer (TA404)
- Darolutamide with androgen deprivation therapy for treating hormone-relapsed nonmetastatic prostate cancer (TA660)
- Apalutamide with androgen deprivation therapy for treating hormone-sensitive metastatic prostate cancer (TA741)
- Darolutamide with androgen deprivation therapy and docetaxel for treating hormonesensitive metastatic prostate cancer (TA903)
- Docetaxel for the treatment of hormone-refractory metastatic prostate cancer (TA101)
- Apalutamide with androgen deprivation therapy for treating high-risk hormonerelapsed non-metastatic prostate cancer (TA740)
- Enzalutamide for treating metastatic hormone-relapsed prostate cancer before chemotherapy is indicated (TA377)

- Olaparib for previously treated BRCA mutation-positive hormone-relapsed metastatic prostate cancer (TA887)
- Abiraterone for castration-resistant metastatic prostate cancer previously treated with a docetaxel-containing regimen (TA259)
- Abiraterone for treating metastatic hormone-relapsed prostate cancer before chemotherapy is indicated (TA387)
- Cabazitaxel for hormone-relapsed metastatic prostate cancer treated with docetaxel (TA391)
- Enzalutamide for metastatic hormone-relapsed prostate cancer previously treated with a docetaxel-containing regimen (TA316)
- Radium-223 dichloride for treating hormone-relapsed prostate cancer with bone metastases (TA412)

Negative NICE Technology Appraisals

- Padeliporfin for untreated localised prostate cancer (TA546)
- Enzalutamide for hormone-relapsed non-metastatic prostate cancer (TA580)
- Abiraterone for treating newly diagnosed high-risk hormone-sensitive metastatic prostate cancer (TA721)