Application Form

^{68}Ga PSMA-11 PET/CT imaging for patients who are candidates for PSMA targeted therapy.

(New and / or Amended

Request for Public Funding)

(Version 2.4)

This application form is to be completed for new and amended requests for public funding (including but not limited to the Medicare Benefits Schedule (MBS)). It describes the detailed information that the Australian Government Department of Health requires to determine whether a proposed medical service is suitable.

Please use this template, along with the associated Application Form Instructions to prepare your application. Please complete all questions that are applicable to the proposed service, providing relevant information only. Applications not completed in full will not be accepted. The separate MSAC Guidelines should be used to guide health technology assessment (HTA) content of the Application Form

Should you require any further assistance, departmental staff are available through the Health Technology Assessment Team (HTA Team) on the email below to discuss the application form, or any other component of the Medical Services Advisory Committee process.

Email: hta@health.gov.au
Website: www.msac.gov.au

PART 1 – APPLICANT DETAILS

1. Applicant details (primary and alternative contacts)

Corporation / partnership details (where relevant): Insert corporation/partnership details here if relevant
Corporation name: Telix Pharmaceuticals Limited
ABN: 85 616 620 369
Business trading name: Telix Pharmaceuticals Limited

Primary contact name: REDACTED

Primary contact numbers
Business: REDACTED
Mobile: REDACTED
Email: REDACTED

Alternative contact name: REDACTED

Alternative contact numbers
Business: REDACTED
Mobile: REDACTED
Email: REDACTED

2. (a) Are you a consultant acting on behalf on an applicant?

☐ Yes
☒ No

(b) If yes what is the Applicant(s) name that you are acting on behalf of?

3. (a) Are you a lobbyist acting on behalf of an Applicant?

☐ Yes
☒ No

(b) If yes, are you listed on the Register of Lobbyists?

☐ Yes
☐ No

(c) Have you engaged a consultant on your behalf?

☒ Yes
☐ No

PART 2 – INFORMATION ABOUT THE PROPOSED MEDICAL SERVICE

4. Application title

^{68}Ga PSMA-11 PET/CT imaging for patients who are candidates for PSMA targeted therapy.

5. Provide a succinct description of the medical condition relevant to the proposed service (no more than 150 words – further information will be requested at Part F of the Application Form)

For Australian men, prostate cancer is the most commonly diagnosed cancer (>19000 cases pa) and the send most common cause of death via cancer (>3000 pa). More than 90,000 Australian men are estimated to be currently living with a diagnosis of prostate cancer, however, although breakthroughs in treatments mean that they are living longer (studies between 1986-1990 and 2011-2015 showed a survival rate increase from 59% to 95%) they are still afflicted with common side effects, such as; depression, anxiety, urinary incontinence, sexual impairments and bowel function impairments.

Overall quality of life for men diagnosed with prostate cancer declines over time, with 35-40% of men experiencing poorer physical and mental health 10 years after diagnosis, due to disease and treatments. The total cost of treating prostate cancer is high and is estimated to be around $500 million in 2013 for persons diagnosed between 2009 and 2013.

^{68}Ga-PSMA-11 is among the most widely used agents for prostate cancer PET/computed tomography (CT) imaging. To date, the use of 68Ga-PSMA has been well reported, and initial staging revealed superior sensitivity and specificity profiles compared to conventional choline-based tracers. Not only diagnosis but also among the management changes observed in the studies, the proportion of inter and intra-modality was relatively similar, indicating that 68Ga-PSMA PET may help better plan the optimal dose, site, and volume of radiation in the case of salvage radiotherapy.

6. Provide a succinct description of the proposed medical service (no more than 150 words – further information will be requested at Part 6 of the Application Form)

ILLUCCIX® is a radiopharmaceutical cold kit manufactured by Telix under cGMP conditions and has a shelf life of 24 months. ILLUCCIX® is a kit for the preparation of ^{68}Ga-PSMA-11 injection. The kit allows for non-invasive positron emission tomography/ computed tomography (PET/CT) for the imaging of prostate specific membrane antigen (PSMA)-expressing colon cancer. PSMA-11 is a synthetic urea-based peptide inhibitor of PSMA, it incorporates a chelate HBED-CC and binds to PSMA. Once PSMA-11 is radio labelled with the radioisotope gallium-68 (^{68}Ga), it results in $_{68}$Ga-PSMA-11, made up to three individual patient doses, which can then be administered to patients intravenously as a PET-tracer to image PSMA-expressing prostate tumours, including metastatic diseases.

The ILLUCCIX® kit contains the necessary components that are needed for nuclear pharmacy preparation of ^{68}Ga-PSMA-11 at ambient temperatures. It is also available in three configurations to support the major commercially available ^{68}Ga generators (EZAG, IRE and ITG).

ILLUCCIX (TLX591-CDx), is a radiopharmaceutical cold kit for the preparation of ^{68}Ga-PSMA-11 injection, for the positron emission tomography (PET) imaging of men with prostate cancer.

ILLUCCIX was granted TGA approval (ARTG 356332 and ARTG 356333) on the 2nd of November 2021 for the PET imaging of men with prostate cancer. Specifically:

1. Who are at risk of metastasis and who are suitable for definitive initial therapy
    a. Primary staging population and
2. Who have suspected recurrence based on elevated serum PSA level.
    a. Biochemical recurrence population

The Sponsor intends to apply to the TGA in March 2022 for an additional indication below which is the subject of this current application.

3. patients who are candidates for PSMA targeted therapy.

Diagnostic accuracy of ^{68}Ga-PSMA-11 PET in men with prostate cancer with metastasis or biochemical recurrence (BCR) based on elevated PSA levels who are candidates for radiotherapy, prostatectomy or PSMA targeted therapy has been reported in multiple studies. A targeted literature search suggests, the key studies for patients who maybe candidate for PSMA targeted therapy are:

VISION Study, PSMA-617-01; An international, prospective, open label, multi-center, randomized Phase 3 study of 177Lu-PSMA-617 in the treatment of patients with progressive PSMA-positive metastatic castration-resistant (Sartor et. al., 2021[1]) and TheraP Study, [177Lu]Lu-PSMA-617 versus cabazitaxel in patients with metastatic castration-resistant prostate cancer (TheraP): a randomised, open-label, phase 2 trial) Hofman et. al., 2021[2]).

A full literature search will be conducted for the application (ADAR) to reveal any further relevant studies.

Telix would like to request to bypass PASC, considering the following Ratified PICOs are available for consultation to proceed directly to preparing an ADAR for submission to MSAC:

- previous application for MSAC Application 1632 (PSMA PET/CT) that has been considered by MSAC and recommended for listing (MSAC 1632 PSD[3] and a Ratified PICO[4]) are available for consultation and
- current application for MSAC Application 1686 (^{177}Lutetium PSMA i&t) has been submitted and a Ratified PICO[5] is available for consultation.

7. (a) Is this a request for MBS funding?

☒ Yes
☐ No

(b) If yes, is the medical service(s) proposed to be covered under an existing MBS item number(s) or is a new MBS item(s) being sought altogether?

☐ Amendment to existing MBS item(s)
☒ New MBS item(s)

(c) If an amendment to an existing item(s) is being sought, please list the relevant MBS item number(s) that are to be amended to include the proposed medical service/technology:

Insert relevant MBS item numbers here

(d) If an amendment to an existing item(s) is being sought, what is the nature of the amendment(s)?

i. ☐ An amendment to the way the service is clinically delivered under the existing item(s)
ii. ☐ An amendment to the patient population under the existing item(s)
iii. ☐ An amendment to the schedule fee of the existing item(s)
iv. ☐ An amendment to the time and complexity of an existing item(s)
v. ☐ Access to an existing item(s) by a different health practitioner group
vi. ☐ Minor amendments to the item descriptor that does not affect how the service is delivered
vii. ☐ An amendment to an existing specific single consultation item
viii. ☐ An amendment to an existing global consultation item(s)
ix. ☐ Other (please describe below):

Insert description of 'other' amendment here

(e) If a new item(s) is being requested, what is the nature of the change to the MBS being sought?

i. ☐ A new item which also seeks to allow access to the MBS for a specific health practitioner group

ii. ☐ A new item that is proposing a way of clinically delivering a service that is new to the MBS (in terms of new technology and / or population)
iii. ☐ A new item for a specific single consultation item
iv. ☐ A new item for a global consultation item(s)

(f) Is the proposed service seeking public funding other than the MBS?

☐ Yes
☒ No

(g) If yes, please advise:

Insert description of other public funding mechanism here

8. What is the type of medical service/technology?

☐ Therapeutic medical service
☒ Investigative medical service
☐ Single consultation medical service
☐ Global consultation medical service
☐ Allied health service
☐ Co-dependent technology
☐ Hybrid health technology

9. For investigative services, advise the specific purpose of performing the service *(which could be one or more of the following)*:

i. ☐ To be used as a screening tool in asymptomatic populations
ii. ☒ Assists in establishing a diagnosis in symptomatic patients
iii. ☐ Provides information about prognosis
iv. ☒ Identifies a patient as suitable for therapy by predicting a variation in the effect of the therapy
v. ☒ Monitors a patient over time to assess treatment response and guide subsequent treatment decisions

10. Does your service rely on another medical product to achieve or to enhance its intended effect?

☐ Pharmaceutical / Biological
☐ Prosthesis or device
☒ No

11. (a) If the proposed service has a pharmaceutical component to it, is it already covered under an existing Pharmaceutical Benefits Scheme (PBS) listing?

☐ Yes
☒ No

(b) If yes, please list the relevant PBS item code(s):

Insert PBS item code(s) here

(c) If no, is an application (submission) in the process of being considered by the Pharmaceutical Benefits Advisory Committee (PBAC)?

☐ Yes (please provide PBAC submission item number below)
☒ No

Insert PBAC submission item number here

(d) If you are seeking both MBS and PBS listing, what is the trade name and generic name of the pharmaceutical?

Trade name: Insert trade name here

Generic name: Insert generic name here

12. (a) If the proposed service is dependent on the use of a prosthesis, is it already included on the Prostheses List?

☐ Yes
☒ No

(b) If yes, please provide the following information (where relevant):

Billing code(s): Insert billing code(s) here
Trade name of prostheses: Insert trade name here
Clinical name of prostheses: Insert clinical name here
Other device components delivered as part of the service: Insert description of device components here

(c) If no, is an application in the process of being considered by a Clinical Advisory Group or the Prostheses List Advisory Committee (PLAC)?

☐ Yes
☒ No

(d) Are there any other sponsor(s) and / or manufacturer(s) that have a similar prosthesis or device component in the Australian market place which this application is relevant to?

☐ Yes
☒ No

(e) If yes, please provide the name(s) of the sponsor(s) and / or manufacturer(s):

Insert sponsor and/or manufacturer name(s) here

13. Please identify any single and / or multi-use consumables delivered as part of the service?

Single use consumables: Insert description of single use consumables here
Multi-use consumables: Insert description of multi use consumables here

PART 3 – INFORMATION ABOUT REGULATORY REQUIREMENTS

14. (a) If the proposed medical service involves use of a medical device, in-vitro diagnostic test, pharmaceutical product, radioactive tracer, or any other type of therapeutic good, please provide details

Type of therapeutic good: Medicine
Manufacturer's name: Telix Pharmaceuticals
Sponsor's name: Telix Pharmaceuticals

Telix is the developer of Illuccix® (TLX591-CDx), which is a radiopharmaceutical cold kit for the preparation of 68Ga-PSMA-11 injection, for the positron emission tomography (PET) imaging of men with prostate cancer. Illuccix was granted TGA approval on the 2nd of November 2021 for the PET imaging of men with prostate cancer:

1. Who are at risk of metastasis and who are suitable for definitive initial therapy, and
2. Who have suspected recurrence based on elevated serum PSA level.

Figure 1: Illuccix® Kit

(b) Has it been listed on the Australian Register of Therapeutic Goods (ARTG) by the Therapeutic Goods Administration (TGA)? If the therapeutic good has been listed on the ARTG, please state the ARTG identification numbers, TGA-approved indication(s), and TGA-approved purpose(s).

TGA approved indication(s), if applicable: If applicable, insert description of TGA approved indication(s) here
TGA approved purpose(s), if applicable: If applicable, insert description of TGA approved purpose(s) here

Telix's diagnostic agent, Illuccix (^{68}Ga-PSMA-11), was approved by the TGA on 2nd November 2021 and the approved PI is available (ILLUCCIX Australian Approved Product Information[6].

Specifically, the current status of TGA registration of Illuccix is:

- Granted priority review status by TGA: 4 December 2020
- TGA Approval: 2 November 2021
- TGA Application ID: Priority submission PM-2021-00851-1-4 glu-urea-lys(ahx)-hbed-cc [pmsa-hbed-cc] (Illuccix).

ARTG ID: 356332

- ILLUCCIX Configuration A Kit for the Preparation of Ga-68 Glu-urea-Lys(ahx)-hbed-CC 25 mcg solution for injection Glass Vial
- **Active ingredients:** Glu-urea-Lys(ahx)-hbed-CC
- **Sponsor:** Telix Pharmaceuticals (ANZ) Pty Ltd

ARTG ID: 356333

- ILLUCCIX Configuration B Kit for the Preparation of Ga-68 Glu-urea-Lys(ahx)-hbed-CC 25 mcg solution for injection Glass Vial
- **Active ingredients:** Glu-urea-Lys(ahx)-hbed-CC
- **Sponsor:** Telix Pharmaceuticals (ANZ) Pty Ltd

ILLUCCIX is supplied as a sterile, multi-dose kit for the preparation of Ga-68 Glu-urea-Lys(ahx)- hbed-CC for intravenous use. There are 2 different kit configurations, each containing 3 vials.

ILLUCCIX Configuration "A" is intended for use with Ga-68 produced from a cyclotron and purified via GE FASTlab™ or Eckert & Ziegler GalliaPharm® Ge 68/Ga-68 generator and includes:

- Vial 1 (Glu-urea-Lys(ahx)-hbed-CC Vial): contains 25 microgram Glu-urea-Lys(ahx)-hbed-CC, 10 microgram mannose and water for injections as a lyophilized powder in a sterile 10 mL vial with a blue flip-off cap.
- Vial 2 (Buffer Vial, Configuration A): contains 150 mg sodium acetate, 0.077 mL hydrochloric acid and water for injections (2.5 mL volume) in a sterile 10 mL vial with a red flip off cap.
- Vial 3 (Sterile Vacuumed Vial): an evacuated sterile vial with white flip off cap used to collect Ga68 chloride from generators or cyclotron.

ILLUCCIX Configuration "B" is intended for use with Ga-68 produced from an IRE Galli Eo® Ge 68/Ga-68 generator and includes:

- Vial 1 (Glu-urea-Lys(ahx)-hbed-CC Vial): contains 25 microgram Glu-urea-Lys(ahx)-hbed-CC, 10 microgram mannose and water for injections as a lyophilized powder in a sterile 10 mL vial with a blue flip-off cap.
- Vial 2 (Buffer Vial, Configuration B): contains 150 mg sodium acetate, 0.15 mL hydrochloric acid and water for injections (6.4 mL volume) in a sterile 10 mL vial with a green flip off cap.
- Vial 3 (Sterile Vacuumed Vial): an evacuated sterile vial with white flip off cap used to collect Ga68 chloride from generator.

The radionuclide is not part of the kit. Before reconstitution and radiolabelling with Ga-68, the contents of this kit are not radioactive.

ILLUCCIX, after radiolabelling with Ga-68, is a radioactive diagnostic agent indicated for use with positron emission tomography (PET) imaging combined with Computerised Tomography (CT) in patients with prostate cancer:

- who are at risk of metastasis and who are suitable for initial definitive therapy.
- who have suspected recurrence based on elevated serum prostate specific antigen (PSA) level.

See answer for Question 15(c) for anticipated submission to the TGA for the current indication related to this application.

- ^{68}Ga PSMA PET/CT imaging for patients who are candidates for PSMA targeted therapy.

(c) If a medical device is involved, has the medical device been classified by TGA as a Class III OR Active Implantable Medical Device (AIMD) under the TGA regulatory scheme for devices?

☐ Class III
☐ AIMD
☒ N/A

(d) Is the therapeutic good classified by TGA for Research Use Only (RUO)?

Product Category: Medicine (see ARTG entries 356332 and 356333).

15. (a) <u>If not listed on the ARTG</u>, is the therapeutic good to be used in the service exempt from the regulatory requirements of the *Therapeutic Goods Act 1989*?

☐ Yes (If yes, please provide supporting documentation as an attachment to this application form)
☐ No

(b) If the therapeutic good is <u>not ARTG listed</u>, is the therapeutic good in the process of being considered by TGA?

☐ **Yes (if yes, please provide details below)**
☐ **No**

Date of submission to TGA: Insert date of submission here
Estimated date by which TGA approval can be expected: Insert estimated date here
TGA Application ID: Insert TGA Application ID here
TGA approved indication(s), if applicable: If applicable, insert description of TGA approved indication(s) here
TGA approved purpose(s), if applicable: If applicable, insert description of TGA approved purpose(s) here

(c) If **the therapeutic good is NOT in the process of being considered by TGA, is an application to TGA being prepared?**

☒ Yes (please provide details below)
☐ No

Estimated date of submission to TGA: REDACTED

Proposed indication(s), if applicable: 68Ga PSMA PET/CT imaging for patients who are candidates for PSMA targeted therapy.

Proposed purpose(s), if applicable: Not applicable

PART 4 – SUMMARY OF EVIDENCE

16. Provide one or more recent (published) high quality clinical studies that support use of the proposed health service/technology. At 'Application Form lodgement', please do not attach full text articles; just provide a summary. .

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
1	Randomsied Controlled Trial	Lutetium-177–PSMA-617 for Metastatic Castration-Resistant Prostate Cancer Name: VISION	International, open-label, phase 3 trial evaluating 177Lu-PSMA-617 in patients who had metastatic castration-resistant prostate cancer previously treated with at least one androgen-receptor–pathway inhibitor and one or two taxane regi-mens and who had PSMA-positive gallium-68 (68Ga)–labeled PSMA-11 positron-emission tomographic–computed tomographic scans.	https://www.nejm.org/doi/10.1056/NEJMoa2107322?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub++0pubmed Sartor et. al., 2021[1]	2021
2	Randomsied Controlled Trial	[177Lu]Lu-PSMA-617 versus cabazitaxel in patients with metastatic castration-resistant prostate cancer (TheraP): a randomised, open-label, phase 2 trial. Name: TheraP	Multicentre, unblinded, randomised phase 2 trial at 11 centres in Australia. Men with mCRPC for whom cabazitaxel was considered the standard treatment. Men underwent [68Ga]Ga-PSMA-11 and 2-flourine-18[18F]FDG) PET with PET eligibility criteria for the trial PSMA-positive disease, and no discordant FDG-sites. 160 men randomised(1:1) to [177Lu]LuPSMA-617 (6·0-8·5 GBq intravenously every 6 weeks for up to six cycles) or cabazitaxel (20 mg/m2) Primary endpoint was prostate-specific antigen (PSA) response. PSA responses were more frequent among men in the [177Lu]Lu-PSMA-617 group than in the cabazitaxel group (65 vs 37 PSA responses;	https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00237-3/fulltext Hofman et. al., 2021[2]	2021

			66% vs 37% by intention to treat; difference 29% p=0·0016).		
3	Randomsied Controlled Trial	Prostate-specific membrane antigen PET- CT in patients with high- risk prostate cancer before curative intent surgery or radiotherapy (proPSMA): a prospective, randomised, multicentrestudy Name: proPSMA	A randomised controlled trial of 300 patients examining the diagnostic accuracy of ^{68}GaPSMA11PET/CT compared to conventional imaging in primary prostate cancer staging prior tocurative intent therapy with respect to diagnostic accuracy and independent and incremental management impact	https://doi.org/10.1016/S0140-6736(20)30314-7 Hofman et. al., 2020[7]	2020
4	Randomsied Controlled Trial (Protocol)	A prospective randomized multicentre study of the impact of gallium-68 prostate-specific membrane antigen (PSMA) PET/CT imaging for staging high-risk prostate cancer prior to curative-intent surgery or radiotherapy (proPSMA study): clinical trial protocol. Name: proPSMA	A randomised controlled trial of 300 patients examining the diagnostic accuracy of ^{68}GaPSMA11PET/CT compared to conventional imaging in primary prostate cancer staging prior tocurative intent therapy with respect to diagnostic accuracy and independent and incremental management impact	https://bjui-journals.onlinelibrary.wiley.com/doi/10.1111/bju.14374 Hofman et. al., 2018[8]	2018
5	Meta-analysisof Management Impact	Impact of ^{68}Ga-PSMA PET on the Managementof Patients with ProstateCancer: A Systematic Review and Meta- analysis	Fifteen studies (1163 patients) were included. The pooled proportion of management changeswas 54% (95% confidence interval 47– 60%). ^{68}Ga-PSMA PET had a large impact on the management of patients with prostate cancer. Greater PET positivity was associated with higher proportion of management changes	https://doi.org/10.1016/j.eururo.2018.03.030 Han et. al., 2018[9]	**2018**
6	Systemic Review and Meta-analysis	Gallium-68 Prostate- specific Membrane Antigen Positron Emission Tomography inAdvanced Prostate Cancer—Updated	37 articles including 4790 patients analysed. Ga-68-PSMA PET improves detection of metastaseswith biochemical	https://www.sciencedirect.com/science/article/abs/pii/S0302283819300958?via%3Dihub	2019

		Diagnostic Utility, Sensitivity, Specificity, and Distribution of Prostate-specific Membrane Antigen-avidLesions: A Systematic Review and Meta- analysis	recurrence, particularly at low pre-PET PSA levels of >0.2 ng/ml (33%) and 0.2–0.5 ng/ml (45%). Significant differences in positivity after biochemical recurrence in the prostate bed were noted between radical prostatectomy (22%) and radiotherapy (52%) patients. On per-node analysis,high sensitivity (75%) and specificity (99%) were observed.	https://doi.org/10.1016/j.eururo.2019.01.049 Perera et. al., 2020[10]	
7	Systemic Review and Meta-analysis	^{68}Ga-Labeled Prostate- specific Membrane Antigen Ligand Positron Emission Tomography/Computed Tomography for Prostate Cancer: A Systematic Review and Meta-analysis	Fifteen ^{68}Ga-PSMA PET/CT studies with 1256 patients met the inclusion criteria. Overall detection rate of 81% and 53% for PSA < .5ng/ml inbiochemical recurrence group. In histologically validated studies FP rate for lymph node metastases 3%	dx.doi.org/10.1016/j.euf.2016.11.002 von Eyben et. al., 2018[11]	2018

** Categorise study design, for example meta-analysis, randomised trials, non-randomised trial or observational study, study of diagnostic accuracy, etc.*

***Provide high level information including population numbers and whether patients are being recruited or in post-recruitment, including providing the trial registration number to allow for tracking purposes.*

**** If the publication is a follow-up to an initial publication, please advise.*

17. **Identify <u>yet-to-be-published</u> research that may have results available in the near future (that could be relevant to your application). Do not attach full text articles; this is just a summary.**

No yet-to-be-published studies have been identified where results would be available in the near future (ie March-July 2022) that could be relevant to this application.

	Type of study design*	**Title of research (including any trial identifier if relevant)**	**Short description of research (max 50 words)****	**Website link to research (if available)**	**Date*****
1.	n/a	n/a	n/a	n/a	n/a

** Categorise study design, for example meta-analysis, randomised trials, non-randomised trial or observational study, study of diagnostic accuracy, etc.*

***Provide high level information including population numbers and whether patients are being recruited or in post-recruitment.*

****Date of when results will be made available (to the best of your knowledge).*

PART 5 – CLINICAL ENDORSEMENT AND CONSUMER INFORMATION

18. List all appropriate professional bodies/organisations representing the health professionals who provide the service. For MBS-related applications ONLY, please attach a brief 'Statement of Clinical Relevance' from the most relevant college/society.

Australian Association of Nuclear Medicine Specialists
The Royal Australian and New Zealand College of Radiologists
Australian and New Zealand Society of Nuclear Medicine
Urological SANZ

These are the peak bodies who represent the only health care professionals who are licensed to provide PET/CT scan services in Australia.

Statement of Clinical Relevance have been sought and will be forward to the MSAC Secretariat under separate email.

19. List any professional bodies / organisations that may be impacted by this medical service (i.e. those who provide the comparator service):

As above

20. List the consumer organisations relevant to the proposed medical service (noting there is NO NEED to attach a support letter at the 'Application Lodgement' stage of the MSAC process):

List relevant consumer organisations here

Prostate Cancer Foundation Australia

21. List the relevant sponsor(s) and / or manufacturer(s) who produce similar products relevant to the proposed medical service:

List relevant sponsor/s and or manufacturer/s here

None

22. Nominate two experts that can be contacted about the proposed medical service, and current clinical management of the condition:

Name of expert 1: REDACTED

Telephone number(s): REDACTED

Email address: REDACTED

Justification of expertise: REDACTED

Name of expert 2: REDACTED

Telephone number(s): REDACTED

Email address: REDACTED

Justification of expertise: REDACTED

Please note that the Department may also consult with other referrers, proceduralists and disease specialists to obtain their insight.

PART 6 – POPULATION (AND PRIOR TESTS), INTERVENTION, COMPARATOR, OUTCOME (PICO)

PART 6a – INFORMATION ABOUT THE PROPOSED POPULATION

23. Define the medical condition, including providing information on the natural history of the condition and a high level summary of associated burden of disease (in terms of both morbidity and mortality):

Currently prostate cancer is the most commonly diagnosed cancer (>19000 cases per annum) and the second most common cause of death (> 3000 per annum) in Australian men. The risk of developing prostate cancer before their 85th birthday is 1 in 6 for Australian men.

More that 90,000 Australian men are estimated to be living with prostate cancer.

Between 1986–1990 and 2011–2015, five-year relative survival from prostate cancer improved from 59% to 95%. This improvement in survival is most likely due to the impact of better diagnosis and treatment on the natural history of the disease.

Prostate Cancer originates in the prostate gland and is most commonly adenocarcinoma in type. Many prostate cancers are indolent by nature and do not affect longevity, particularly in older men with significant co-morbidities. However, untreated prostate cancers grow locally and can reach a size where men experience difficulty and/or discomfort urinating and blood in the urine or sperm. Over time, if untreated, prostate cancer spreads to other tissues such as lymph nodes, bones, lungs and liver and can lead to bone pain, spinal cord compression, weight loss, fatigue, shortness of breath and is ultimately fatal.

By the time symptoms have developed prostate cancer is most commonly incurable. Screening by digital rectal examination is very insensitive for detecting early stage curable disease.

With the advent of Prostate Specific Antigen Testing (PSA) earlier diagnosis has been facilitated and currently nearly 80% of patients have Stage 1 or 2 disease at diagnosis with a high chance of cure using loco-regional treatments such as radical prostatectomy and radiotherapy. Five-year survival rates are currently in excess of 95% for patients with Stage 1-3 disease. For patients diagnosed with prostate cancer in 2011, only 4% of patients had Stage IV disease (distant metastases) that is currently incurable, leading to a reduction in 5 year survival to 36% in this group.

Men with prostate cancer are living longer, but not necessarily living well. Quality of life declines over time with 35–40% of men experiencing poorer physical and mental quality of life outcomes and life satisfaction 10 years after the diagnosis due to effects of the disease and treatment. Depression, anxiety, urinary incontinence, and impairments in sexual and bowel function are common.

The cost of treating prostate cancer is also high, estimated to be $500 million in 2013 for persons diagnosed between 2009 and 2013 and this doesn't include costs paid by patients themselves. These estimates also do not incorporate the cost of more advanced and more expensive androgen deprivation drugs introduced into clinical practice in the last 5 years.

24. Specify the characteristics of patients with (or suspected of having) the medical condition, who would be eligible for the proposed medical service/technology (including details on how a patient would be

investigated, managed and referred within the Australian health care system, in the lead up to being eligible for the service):

^{68}Ga PSMA PET/CT imaging for patients who are candidates for PSMA targeted therapy, ie patients who have metastatic castrate resistant prostate cancer (mCRPC).

PART 6b – INFORMATION ABOUT THE INTERVENTION

25. Describe the key components and clinical steps involved in delivering the proposed medical service/technology:

The overall procedure for ^{68}Ga PSMA PET/CT scanning is very similar to currently MBS funded PET/CT procedures, although fasting is not required.

When men are referred for a ^{68}Ga PSMA PET/CT scan, the clinical need for the diagnostic procedure is verified by an experienced healthcare professional and if the request is valid an appointment is made so that supply of the short-lived radiotracer can be organised for an appropriate time. The patient is given details about the scan and necessary preparation

On the day of the scan the ^{68}Ga PSMA is administered intravenously and 45-120 minutes later a PET/CT scan is performed. The imaging time is approximately 30 minutes during which time the patient can lie comfortably on the scanning bed. Upon completion the patient can leave the imaging facility without further requirements. Adverse events are extraordinarily rare when these diagnostic agents are administered

The scan is interpreted by an appropriately credentialled specialist and their report is provided to the referring specialist who incorporates the information gained into the patient's management plan

26. Does the proposed medical service include a registered trademark component with characteristics that distinguishes it from other similar health components?

Insert description of registered trademark component here

Trade mark is ILLUCCIX (see previous section for notes on ARTG ID: 356333 and ARTG ID: 356332).

ARTG ID: 356333 and

- ILLUCCIX Configuration B Kit for the Preparation of Ga-68 Glu-urea-Lys(ahx)-hbed-CC 25 mcg solution for injection Glass Vial
- **Active ingredients:** Glu-urea-Lys(ahx)-hbed-CC
- **Sponsor:** Telix Pharmaceuticals (ANZ) Pty Ltd

ARTG ID: 356332

- ILLUCCIX Configuration A Kit for the Preparation of Ga-68 Glu-urea-Lys(ahx)-hbed-CC 25 mcg solution for injection Glass Vial
- **Active ingredients:** Glu-urea-Lys(ahx)-hbed-CC

Sponsor: Telix Pharmaceuticals (ANZ) Pty Ltd

ILLUCCIX after radiolabelling with ^{68}Ga, is a radioactive PSMA diagnostic agent.

27. If the proposed medical service has a prosthesis or device component to it, does it involve a new approach towards managing a particular sub-group of the population with the specific medical condition?

Insert description of approach here

Not applicable

28. If applicable, are there any limitations on the provision of the proposed medical service delivered to the patient (i.e. accessibility, dosage, quantity, duration or frequency)?

If applicable, insert description of limitations here

None

29. If applicable, identify any healthcare resources or other medical services that would need to be delivered <u>at the same time</u> as the proposed medical service:

If applicable, insert description of resources or other medical services here

Access to PSMA PET/CT scans is limited by the number or PET/CT sites[1] (currently approximately 92 sites throughout Australia (Australian Government 2021)[12].

30. If applicable, advise which health professionals will primarily deliver the proposed service:

If applicable, insert description of professionals here

Nuclear Medicine Technologists

Medical Physicists

Radiochemists and radiopharmacists

Nuclear Medicine Physicians

Radiologists

31. If applicable, advise whether the proposed medical service could be delegated or referred to another professional for delivery:

Insert key components and clinical steps here

No

32. If applicable, specify any proposed limitations on who might deliver the proposed medical service, or who might provide a referral for it:

If applicable, insert specification of limitations here

Supplied only by medical specialists who are credentialled to deliver PET services, only on referral by a specialist medical practitioner.

33. If applicable, advise what type of training or qualifications would be required to perform the proposed service, as well as any accreditation requirements to support service delivery:

If applicable, insert advice regarding training or qualifications

As above

34. (a) Indicate the proposed setting(s) in which the proposed medical service will be delivered (select <u>ALL</u> relevant settings):

☐ Inpatient private hospital (admitted patient)
☐ Inpatient public hospital (admitted patient)
☐ Private outpatient clinic

[1] PET unit locations by Australian state and territory https://www1.health.gov.au/internet/main/publishing.nsf/Content/pet-unit-locations

☐ Public outpatient clinic
☐ Emergency Department
☐ Private consulting rooms - GP
☐ Private consulting rooms – specialist
☐ Private consulting rooms – other health practitioner (nurse or allied health)
☐ Private day surgery clinic (admitted patient)
☐ Private day surgery clinic (non-admitted patient)
☐ Public day surgery clinic (admitted patient)
☐ Public day surgery clinic (non-admitted patient)
☐ Residential aged care facility
☐ Patient's home
☐ Laboratory
☒ Other – please specify below

Specify further details here

The service will be provided in facilities specifically licensed to undertake PET/CT imaging.

These are located in public and private hospitals are well as stand-alone facilities throughout Australia.

(b) Where the proposed medical service is provided in more than one setting, please describe the rationale related to each:

Describe rationale here

Not applicable

35. Is the proposed medical service intended to be entirely rendered in Australia?

☒ Yes
☐ No – please specify below

Specify further details here

PART 6c – INFORMATION ABOUT THE COMPARATOR(S)

36. Nominate the appropriate comparator(s) for the proposed medical service (i.e. how is the proposed population currently managed in the absence of the proposed medical service being available in the Australian health care system). This includes identifying health care resources that are needed to be delivered at the same time as the comparator service):

In patients who are candidates for PSMA targeted therapy.

Comparator: No ^{68}Ga PSMA-11 PET/CT imaging.

37. Does the medical service (that has been nominated as the comparator) have an existing MBS item number(s)?

☐ Yes (please list all relevant MBS item numbers below)
☒ No

Specify item number/s here

However, noted is MSAC Application 1632 Public Summary Document where MSAC has recommended radiopharmaceutical tracer-agnostic MBS item descriptors for PSMA PET/CT (not ^{68}Ga specific) for which MBS Item number(s) have not yet been listed (as of 1st March 2022).

MSAC Application 1632 PSD: http://www.msac.gov.au/internet/msac/publishing.nsf/Content/1632-public[3]

38. (a) Will the proposed medical service/technology be used in addition to, or instead of, the nominated comparator(s)?

☒ In addition to (i.e. it is an add-on service)
☐ Instead of (i.e. it is a replacement or alternative)

^{68}Ga PSMA-11 PET/CT imaging is not currently being performed.

(b) If yes, please outline the extent to which the current service/comparator is expected to be substituted

Outline service/comparator substitution here

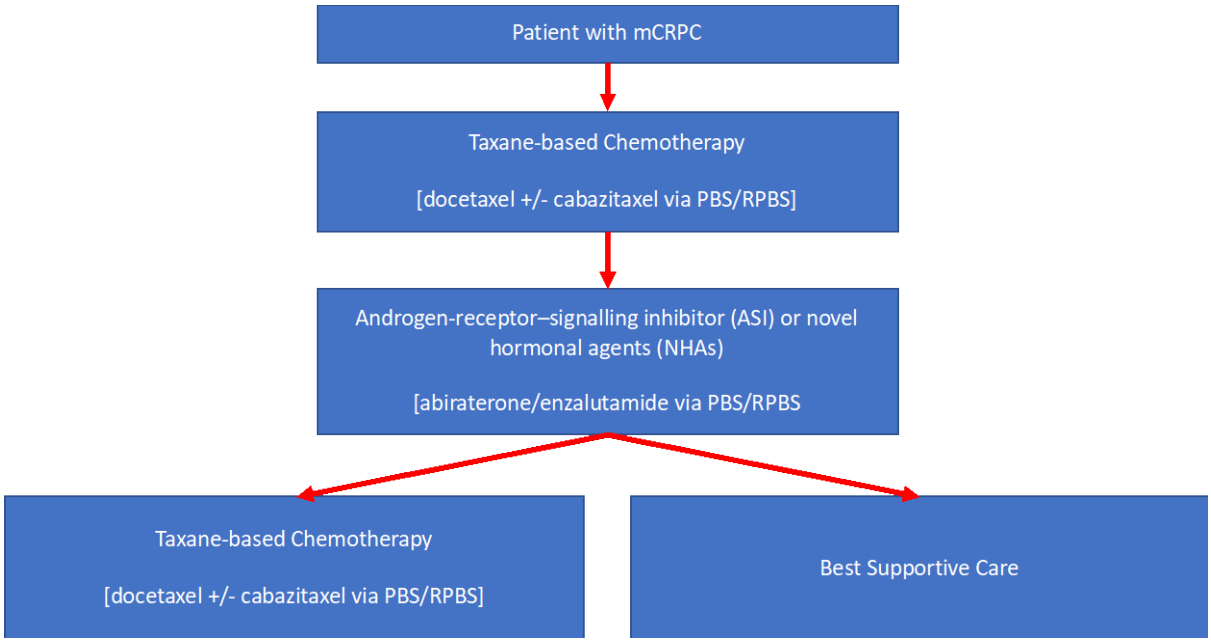
PART 6c CONTINUED – INFORMATION ABOUT ALGORITHMS (CLINICAL MANAGEMENT PATHWAYS)s

39. Define and summarise the CURRENT clinical management pathway (algorithm) that patients follow when they receive the COMPARATOR service (i.e. the landscape before the proposed service is introduced). An easy-to-follow flowchart is preferred, depicting the current clinical management pathway), but dot-points would be acceptable. Please include health care resources used in the current landscape (e.g. pharmaceuticals, diagnostics and investigative services, etc.).

Define and summarise the current clinical management pathways here

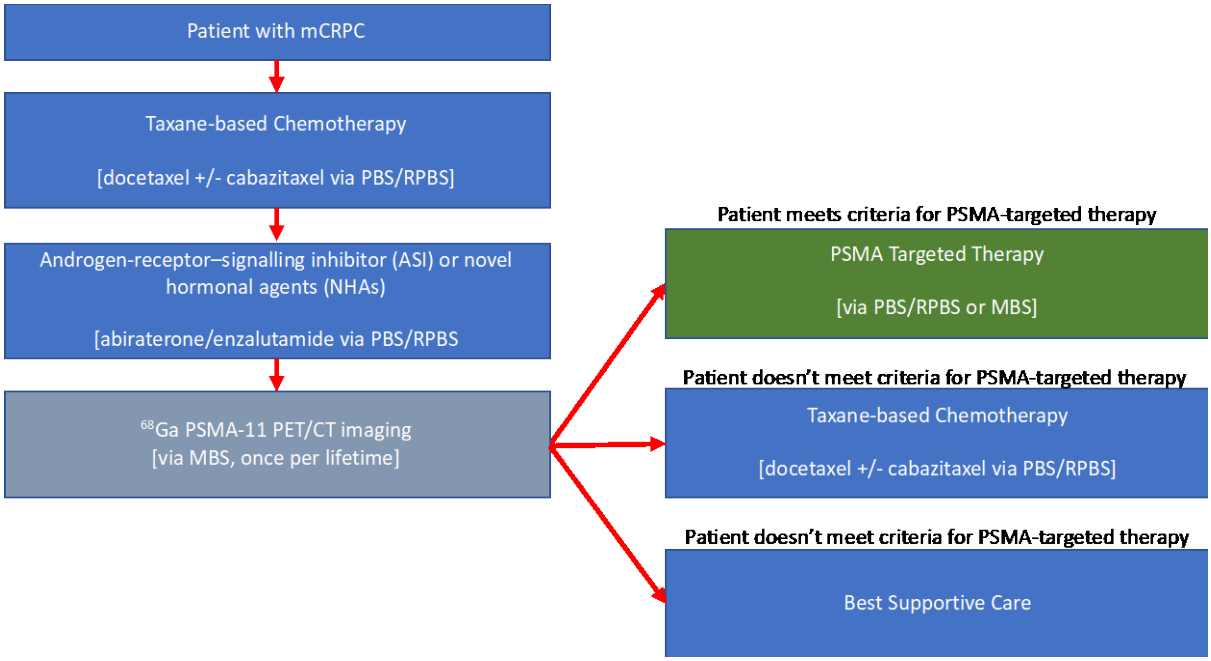
^{68}Ga PSMA PET/CT imaging for patients who are candidates for PSMA targeted therapy.

Figure 1 Simplified current clinical management algorithm for patients who are candidates for PSMA targeted therapy



40. Define and summarise the PROPOSED clinical management pathway (algorithm) that patients would follow <u>after</u> the proposed service/technology is introduced, including variation in health care resources.

Figure 2 Simplified proposed clinical management algorithm for algorithm for patients who are candidates for PSMA targeted therapy



<u>PART 6d – INFORMATION ABOUT CLINICAL OUTCOMES</u>

41. Summarise the clinical claims for the proposed medical service against the appropriate comparator(s), in terms of consequences for health outcomes (comparative benefits and harms):

Summarise clinical claims here

In patients who are candidates for PSMA targeted therapy after identification via ^{68}Ga PSMA PET/CT imaging is superior to no ^{68}Ga PSMA PET/CT imaging in terms of analytical, clinical validity and clinical utility.

42. Please state what the overall clinical claim is:

State overall clinical claim

Overall clinical claim is superiority versus the comparator.

43. List the key health outcomes (major and minor – prioritising major key health outcomes first) that will need to be measured in assessing the clinical claim for the proposed medical service/technology (versus the comparator):

List the key health outcomes here

Safety outcomes

- Radiation exposure (patients, nuclear medicine technologists, nurses).
- Adverse reaction to the contrast agents, including renal toxicity.

Effectiveness outcomes

Diagnostic accuracy

- Sensitivity and specificity
- Positive predictive value (PPV), negative predictive value (NPV)
- Area under the curve (AUC) of the receiver operating characteristic (ROC) curve

Change in management

- Need for subsequent diagnostic tests, including biopsy i.e. investigations avoided
- Change in planned management (intent), including change in planned treatment modality, extension of radiation field
- Change in management i.e. overall change, types of changes, futile locoregional curative intent treatments avoided, therapies instigated

Healthcare system outcomes

- Cost of ^{68}Ga PSMA PET/CT (or comparator) imaging used
- Cost of additional imaging tests or biopsies required
- Cost of treatments received and/or costs offset due to avoidance of futile locoregional ablative procedure
- Total cost to Medicare Benefits Schedule (MBS), Pharmaceutical Benefits Scheme (PBS) and other government health budgets

Economic outcomes

Cost effectiveness

PART 7 – INFORMATION ABOUT ESTIMATED UTILISATION

44. Estimate the prevalence and/or incidence of the condition in the proposed population:

Insert prevalence and/or incidence here

Estimated that the total incident population of patients who may benefit from the ILLUCCIX® Kit to be approximately 12,900 men, and specifically, for the current application:

- Patient Selection for PSMA Targeted Radioligand Therapy (N = 1,540)

45. Estimate the number of times the proposed medical service/technology would be delivered to a patient per year:

Insert estimate here

Patient Selection for PSMA Targeted Radioligand Therapy

a. One ^{68}Ga PSMA-11 scan per lifetime

46. How many years would the proposed medical service/technology be required for the patient?

Once

47. Estimate the projected number of patients who will utilise the proposed medical service(s) for the first full year:

Proposed number of patients that that would utilise the service in first year is approximately 1,540, but this will be further analysed in the application.

48. Estimate the anticipated uptake of the proposed medical service/technology over the next three years, factoring in any constraints in the health system in meeting the needs of the proposed population (such as supply and demand factors), as well as provide commentary on risk of 'leakage' to populations not targeted by the service.

Insert estimate here

A detailed analysis of likely extent of use of ^{68}Ga PSMA-11 scans in the population of patients outlined will be presented in the applicant-developed assessment report (ADAR) that will be lodged with MSAC.

The risk of use beyond the proposed population is low given that it is highly unlikely the product would be used in patients other than those for whom eligibility criteria for funding is sought.

PART 8 – COST INFORMATION

49. Indicate the likely cost of providing the proposed medical service. Where possible, please provide overall cost and breakdown:

The approximate unit cost of the two most widely available cGMP grade ^{68}Ga generators (supplied by IRE Elit and Eckert & Ziegler) is A$110,000. While non-cGMP, technical grade ^{68}Ga generators are available in Australia at a much lower price point (A$40,000), such non-cGMP ^{68}Ga generators are not validated for microbiological sterility and are labelled as being not for in-human use. Thus, the use of such generators is considered unsafe.

Both cGMP grade ^{68}Ga generators mentioned above, have a useful life of approximately nine months and deliver approximately redacted ^{68}Ga elutions (doses) over the duration of their useful life. Thus, the cost of each dose of ^{68}Ga required to radiolabel the ILLUCCIX ® Kit is approximately A$redacted

Table 1 below provides cost of providing ^{68}GaPSMA-11 PET/CT medical service.

Table 1: Cost per ^{68}Ga-PSMA-11 PET/CT Scan

Item	Cost
PSMA-11 Kit (ILLUCCIX®)	$redacted
^{68}Ga[1]	$redacted
PET-CT Scan	$900
Other	n/a
MBS Item Total	$1,945

Notes:

1. A Good Manufacturing Practice (GMP) grade ^{68}Ga generator costs approximately $110,000 and has a useful lifetime of ~9 months. During this lifetime, a ^{68}Ga generator can produce approximately redacted patient doses per 9 months (i.e., $redacted/scan).

50. Specify how long the proposed medical service/technology typically takes to perform:

Specify duration here

It is estimated that the total time is 2-3 hours total from preparation and injection of radiotracer to completion of the PET/CT imaging.

51. If public funding is sought through the MBS, please draft a proposed MBS item descriptor to define the population and usage characteristics that defines eligibility for the medical service/technology.

Patient Selection for PSMA Targeted Radioligand Therapy

Category 5 – DIAGNOSTIC IMAGING SERVICES
MBS [item number] Whole body ^{68}Ga prostate-specific membrane antigen (^{68}Ga-PSMA) positron emission tomography (PET)/computerised tomography (CT) study, performed for the patient selection for PSMA targeted radioligand therapy Applicable only once per lifetime Fee: $1,945

52. If public funding is sought through an alternative (non-MBS) funding arrangement, please draft a service description to define the population and usage characteristics that defines eligibility for the service/technology.

Not applicable.

Proposed item descriptor: insert proposed item descriptor here Fee: $(insert proposed fee here)

PART 9 – FEEDBACK

The Department is interested in your feedback.

53. How long did it take to complete the Application Form?

Insert approximate duration here

54. (a) Was the Application Form clear and easy to complete?

☐ Yes
☐ No

(b) If no, provide areas of concern:

Describe areas of concern here

55. (a) Are the associated Guidelines to the Application Form useful?

☐ Yes
☐ No

(b) If no, what areas did you find not to be useful?

Insert feedback here

56. (a) Is there any information the Department should consider in the future, relating to questions contained or not contained in this Application Form?

☐ Yes
☐ No

(b) If yes, please advise:

Insert feedback here

PART 10 – REFERENCES

1. Sartor O, de Bono J, Chi KN, et al. Lutetium-177-PSMA-617 for Metastatic Castration-Resistant Prostate Cancer. N Engl J Med 2021;385(12):1091-1103. DOI: 10.1056/NEJMoa2107322.
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3. MSAC 1632 Public Summary Document. MSAC 1632 Public Summary Document. 2021. Application 1632 – PSMA PET/CT imaging for informing treatment of patients with prostate cancer. . 2021 (http://www.msac.gov.au/internet/msac/publishing.nsf/Content/B2B42D6E89D50ED8CA258570001ED449/$File/1632%20Final%20PSD%20-%20July%202021.pdf).
4. MSAC 1632 Ratified PICO Confirmation. MSAC 1632 Ratified PICO Confirmation. 2020. PSMA PET/CT imaging for informing treatment of patients with Prostate Cancer. . 2021 (http://www.msac.gov.au/internet/msac/publishing.nsf/Content/B2B42D6E89D50ED8CA258570001ED449/$File/1632%20Ratified%20PICO.pdf).

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8. Hofman MS, Murphy DG, Williams SG, et al. A prospective randomized multicentre study of the impact of gallium-68 prostate-specific membrane antigen (PSMA) PET/CT imaging for staging high-risk prostate cancer prior to curative-intent surgery or radiotherapy (proPSMA study): clinical trial protocol. BJU Int 2018;122(5):783-793. DOI: 10.1111/bju.14374.

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10. Perera M, Papa N, Roberts M, et al. Gallium-68 Prostate-specific Membrane Antigen Positron Emission Tomography in Advanced Prostate Cancer-Updated Diagnostic Utility, Sensitivity, Specificity, and Distribution of Prostate-specific Membrane Antigen-avid Lesions: A Systematic Review and Meta-analysis. Eur Urol 2020;77(4):403-417. DOI: 10.1016/j.eururo.2019.01.049.

11. von Eyben FE, Picchio M, von Eyben R, Rhee H, Bauman G. (68)Ga-Labeled Prostate-specific Membrane Antigen Ligand Positron Emission Tomography/Computed Tomography for Prostate Cancer: A Systematic Review and Meta-analysis. Eur Urol Focus 2018;4(5):686-693. DOI: 10.1016/j.euf.2016.11.002.

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