

MSAC Application 1830

Genetic testing to identify homologous recombination repair (HRR) gene alterations in patients with metastatic castration-sensitive prostate cancer (mCSPC) to determine eligibility for treatment with PBS subsidised talazoparib.

PICO Set

Population

Describe the population in which the proposed health technology is intended to be used:

Adult patients with metastatic castration-sensitive prostate cancer (mCSPC) whose tumours harbour homologous recombination repair (HRR) gene alterations and who may be eligible for a relevant treatment under the Pharmaceutical Benefits Scheme (PBS).

Specify any characteristics of patients with, or suspected of having, the medical condition, who are proposed to be eligible for the proposed health technology, describing how a patient would be investigated, managed and referred within the Australian health care system in the lead up to being considered eligible for the technology:

Prostate cancer is the most commonly diagnosed cancer in Australian men, with an estimated 28,868 new cases in 2025 (a 1 in 5 risk by age 85; AIHW, Cancer Data in Australia, 2025). Five-year relative survival has risen to 96% (2017–2021) but remains strongly stage-dependent: close to 100% for localised disease, falling to approximately 36% at metastatic (Stage IV) disease. National stage-at-diagnosis data (2011) recorded ~4.2% metastatic at diagnosis, though this predates routine PSMA-PET imaging and now likely understates the metastatic population. Despite improvements in diagnosis and treatment, prostate cancer remains a major cause of cancer mortality in Australia, with more than 3,500 deaths annually.

Metastatic castration-sensitive prostate cancer (mCSPC) is an advanced disease state in which tumour growth remains responsive to androgen deprivation therapy (ADT). In recent years, treatment intensification with androgen receptor pathway inhibitors (ARPIs) and chemotherapy has substantially improved outcomes in mCSPC. Despite advances in treatment, metastatic prostate cancer remains associated with substantial morbidity and mortality. Increasingly, molecular biomarkers are being incorporated into treatment decision-making to identify patient subgroups who may derive benefit from targeted therapies. (Parker et al. 2020; NCCN Guidelines; Fizazi et al. 2022; Armstrong et al. 2019).

Approximately 25–30% of patients with metastatic prostate cancer harbour alterations in genes involved in homologous recombination repair (HRR) pathways (Abida, 2017, Armenia, 2018, Chung, 2019). These include BRCA1, BRCA2, ATM, PALB2, CDK12 and other genes involved in DNA damage repair pathways. Identification of HRR gene alterations has become increasingly important with the development of biomarker-directed treatment strategies.

Inherited mutations in several DNA damage repair genes have been reported to predispose men to prostate cancer. Alterations in BRCA1 and BRCA2 are among the most commonly identified HRR gene alterations in metastatic prostate cancer, with BRCA1/2 alterations estimated to occur in approximately 7% of Australian patients with metastatic prostate cancer (MSAC Applications 1618 and 1765).

Early-stage prostate cancer is often asymptomatic, whereas patients with advanced disease may present with urinary symptoms, haematuria, erectile dysfunction or symptoms related to metastatic disease, including bone pain. Patients with mCSPC generally experience a greater symptom burden and poorer functional outcomes than those with non-metastatic disease (Holmstrom et al. 2019). Bone is the predominant site of metastatic spread in prostate cancer and is associated with substantial morbidity, including pain, pathological fractures and spinal cord compression (Kirby et al. 2011; Gandaglia et al. 2015).

Patients with suspected prostate cancer are typically investigated using prostate-specific antigen (PSA) testing, digital rectal examination (DRE), multiparametric magnetic resonance imaging (mpMRI) and prostate biopsy to establish a diagnosis (NCCN Guidelines 2022; Australian Government, Cancer Australia, 2017). Following diagnosis, staging investigations including computed tomography (CT), magnetic resonance imaging (MRI), bone scan and increasingly PSMA-PET may be used to determine disease stage and identify metastatic disease (Australian Government, Cancer Australia, 2017). Patients diagnosed with mCSPC are generally managed by a specialist multidisciplinary team and receive standard systemic treatment including androgen deprivation therapy (ADT), androgen receptor pathway inhibitors (ARPIs) and, where appropriate, docetaxel.

Localised stage prostate cancer can be cured with surgery or radiotherapy, but some patients will relapse with either overt metastases or an isolated rise in PSA. A proportion of these patients are found to have a local relapse and can have salvage therapy (generally radiation), but the remainder of cases are considered to have incurable advanced disease. There is also a proportion of men who have metastases when the prostate cancer is first diagnosed.

For patients who have already been diagnosed with prostate cancer, serial PSA testing, imaging investigations and clinical assessment may be used to monitor patients for disease progression following radical treatment or recurrence (Parker et al, 2020).

Metastatic CSPC is diagnosed when metastatic disease is identified in patients whose disease remains responsive to androgen deprivation therapy. Imaging modalities such as CT, MRI, bone scan and increasingly PSMA-PET are used to detect metastatic disease and determine disease extent. Patients with mCSPC are typically managed by specialist multidisciplinary teams and undergo ongoing clinical assessment and monitoring in accordance with contemporary clinical practice.

Provide a rationale for the specifics of the eligible population:

This application concerns patients with metastatic castration-sensitive prostate cancer (mCSPC), a stage of advanced disease in which cancer has spread beyond the prostate but remains responsive to androgen deprivation therapy. Despite advances in treatment, patients with metastatic disease experience substantially poorer outcomes than those with localised disease.

The proposed testing strategy is intended to identify patients whose tumours harbour pathogenic alterations in homologous recombination repair (HRR) genes, including alterations in BRCA1, BRCA2 and other clinically relevant HRR gene alterations. Identification of HRR gene alterations is proposed to inform selection of patients with mCSPC who may be eligible for treatment with talazoparib in combination with enzalutamide under the Pharmaceutical Benefits Scheme (PBS).

The Phase III TALAPRO-3 study evaluated talazoparib in combination with enzalutamide in patients with mCSPC whose tumours harboured alterations in HRR genes. Patients were prospectively identified using molecular testing for HRR gene alterations, consistent with the biomarker-defined population evaluated in the study. The trial supports the clinical relevance of HRR gene alteration testing in mCSPC and provides the rationale for identifying patients who may be eligible for treatment under the PBS.

In TALAPRO-3, eligibility was determined using the FoundationOne Liquid CDx assay (and FoundationOne CDx tumour tissue testing in certain circumstances). Patients were required to harbour an alteration in at least one pre-specified HRR gene from a 12-gene panel comprising ATM, ATR, BRCA1, BRCA2, CDK12, CHEK2, FANCA, MLH1, MRE11A, NBN, PALB2 and RAD51C.

Patients were stratified by BRCA versus non-BRCA alteration status at randomisation. The proposed testing strategy is intended to identify the same biomarker-defined population evaluated in TALAPRO-3, supporting alignment between the population selected for treatment and the population in which the clinical benefits of talazoparib in combination with enzalutamide were demonstrated.

Are there any prerequisite tests?

Yes

Are the prerequisite tests MBS funded?

Yes

Please provide details to fund the prerequisite tests:

Provide a response if you answered 'No' to the question above

N/A

Intervention

Name of the proposed health technology:

The proposed health technology is the existing BRCA testing service — MBS items 73303 (tumour/somatic) and 73304 (germline) — with the descriptors amended to (i) extend the eligible population from mCRPC to mCSPC and (ii) report the full 12-gene HRR panel (from BRCA1/2 alone), performed by next-generation sequencing (NGS) (companion diagnostic FoundationOne Liquid CDx). The co-dependent therapy for which eligibility is determined is talazoparib (0.5 mg) in combination with enzalutamide (160 mg), based on TALAPRO-3.

Describe the key components and clinical steps involved in delivering the proposed health technology:

HRR gene alterations may be either germline or somatic. Germline alterations are inherited and present in all cells of the body, whereas somatic alterations arise within tumour cells during the development of cancer. Current MBS items 73303 and 73304 support testing for BRCA1/2 alterations in patients with mCRPC to determine eligibility for treatment under the PBS.

The proposed amendment does not introduce a new testing methodology. Rather, it extends the existing testing pathway to identify a broader range of clinically relevant homologous recombination repair (HRR) gene alterations in patients with mCSPC. In TALAPRO-3, patients were prospectively identified using molecular testing and were required to harbour an alteration in at least one of 12 pre-specified HRR genes: ATM, ATR, BRCA1, BRCA2, CDK12, CHEK2, FANCA, MLH1, MRE11A, NBN, PALB2 and RAD51C.

The proposed amendment can therefore be delivered using existing laboratory infrastructure, expertise and quality assurance processes currently used for genomic testing in prostate cancer.

The key clinical steps involved in delivering the proposed HRR testing are summarised as follows:

- Patient diagnosed with metastatic castration-sensitive prostate cancer (mCSPC) and considered for systemic treatment.
- Tumour tissue and/or blood sample collected and submitted to an accredited pathology laboratory.
- Genomic testing performed using established next-generation sequencing (NGS)-based testing methods.
- Analysis undertaken to identify homologous recombination repair (HRR) gene alterations, including BRCA1, BRCA2 and other clinically relevant HRR genes.
- Results interpreted and reported by appropriately qualified molecular pathologists.
- Results provided to the treating specialist to inform treatment selection and identify patients who may be eligible for relevant PBS-funded therapies.

Identify how the proposed technology achieves the intended patient outcomes:

Genetic testing for patients with mCSPC has the potential to improve outcomes by identifying HRR gene alterations and thereby identifying a biomarker-defined population that may benefit from targeted therapy. Identification of HRR gene alterations informs treatment selection and enables identification of patients who may be eligible for relevant treatment under the PBS.

In the Phase III TALAPRO-3 trial, patients were prospectively identified using molecular testing and were required to harbour an alteration in at least one of 12 pre-specified HRR genes. The study therefore evaluated a biomarker-defined population selected on the basis of HRR gene alteration

status. The proposed amendment seeks to identify the same HRR-altered population in clinical practice, supporting alignment between the population selected for treatment and the population in which the clinical benefits of treatment were demonstrated. The study demonstrated clinically meaningful improvements in radiographic progression-free survival (rPFS), supporting the clinical utility of HRR gene alteration testing in patients with mCSPC. By enabling identification of patients with HRR gene alterations, the proposed testing strategy has the potential to improve treatment selection and patient outcomes while supporting a precision medicine approach to the management of metastatic prostate cancer.

Does the proposed health technology include a registered trademark component with characteristics that distinguishes it from other similar health components?

No

The proposed health technology is a molecular diagnostic testing service and does not include a registered trademark component that distinguishes it from other similar health technologies. Testing may be performed using a range of validated laboratory platforms, reagents and commercial kits, some of which may be associated with registered trademarks. However, the proposed health technology is not dependent on any specific proprietary platform or trademarked component.

Explain whether it is essential to have this trademark component or whether there would be other components that would be suitable:

Provide a response if you answered 'Yes' to the question above

Are there any proposed limitations on the provision of the proposed health technology delivered to the patient (For example: accessibility, dosage, quantity, duration or frequency):

No

Provide details and explain:

Provide a response if you answered 'No' to the question above

It is unlikely that a patient would require more than one tumour or germline HRR gene alteration test, as testing would generally be expected to occur once per patient.

BRCA1/2 testing is currently funded under MBS items 73303 and 73304 for mCRPC and is routinely performed in accredited Australian pathology laboratories. The proposed amendment does not introduce a new testing methodology and can be delivered using existing laboratory infrastructure and expertise used for genomic testing in prostate cancer.

If applicable, advise which health professionals will be needed to provide the proposed health technology:

Testing to identify HRR gene alterations should be conducted and the results interpreted and reported by suitably qualified and trained molecular pathologists. Testing should be conducted in specialist laboratories holding the appropriate accreditation.

If applicable, advise whether delivery of the proposed health technology can be delegated to another health professional:

If applicable, provide a description of any related health professionals here

N/A

If applicable, advise if there are any limitations on which health professionals might provide a referral for the proposed health technology:

If applicable, provide a description of any related health professionals here

Addressed above

Is there specific training or qualifications required to provide or deliver the proposed service, and/or any accreditation requirements to support delivery of the health technology?

Yes

Provide details and explain:

Testing to identify HRR gene alterations in patients with mCSPC should be based on a referral request from a specialist or consultant physician and should not be pathologist determinable.

Genomic testing for HRR gene alterations in prostate cancer is currently being performed in accredited Australian pathology laboratories that participate in the Royal College of Pathologists of Australasia (RCPA) Quality Assurance Programs. Further information is available from the RCPA Quality Assurance Programs website: <https://www.rcpaqap.com.au/home-page>

Indicate the proposed setting(s) in which the proposed health technology will be delivered: (select all relevant settings)

- ☐ Consulting rooms
- ☐ Day surgery centre
- ☐ Emergency Department
- ☐ Inpatient private hospital
- ☐ Inpatient public hospital
- ☒ Laboratory
- ☐ Outpatient clinic
- ☐ Patient's home
- ☐ Point of care testing
- ☐ Residential aged care facility
- ☐ Other (please specify)

Is the proposed health technology intended to be entirely rendered inside Australia?

Yes

Please provide additional details on the proposed health technology to be rendered outside of Australia: N/A

Comparator

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:

No HRR gene alteration testing in the mCSPC setting. Patients with mCSPC are currently managed using standard treatment approaches, including androgen deprivation therapy (ADT) in combination with an androgen receptor pathway inhibitor (ARPI) and, where appropriate, docetaxel. Molecular testing to identify HRR gene alterations is not routinely performed to inform treatment selection in mCSPC.

List any existing MBS item numbers that are relevant for the nominated comparators:

MBS item numbers 73303 and 73304 - BRCA1/2 somatic or germline mutation testing is currently funded in mCRPC to determine eligibility for a relevant treatment under the PBS. No MBS-funded HRR gene alteration testing is currently available in the mCSPC setting, and no genetic testing is required for the use of androgen receptor pathway inhibitors (ARPIs) in mCSPC.

Please provide a rationale for why this is a comparator:

No HRR gene alteration testing is currently funded or routinely performed in the mCSPC setting to inform treatment selection. Patients with mCSPC are currently managed using standard systemic treatment approaches, including androgen deprivation therapy (ADT) in combination with an androgen receptor pathway inhibitor (ARPI) and, where appropriate, docetaxel. As treatment selection in mCSPC is not currently guided by HRR gene alteration status, the absence of HRR testing represents current Australian clinical practice.

MBS items 73303 and 73304 currently support BRCA1/2 testing in patients with mCRPC to determine eligibility for treatment under the PBS. The proposed amendment would extend molecular testing to identify HRR gene alterations in the mCSPC setting. Accordingly, current management without HRR testing represents the most appropriate comparator for assessing the clinical utility and impact of the proposed HRR testing strategy.

Pattern of substitution – Will the proposed health technology wholly replace the proposed comparator, partially replace the proposed comparator, displace the proposed comparator or be used in combination with the proposed comparator? (please select your response)

- ☒ None (*used with the comparator*)
- ☐ Displaced (*comparator will likely be used following the proposed technology in some patients*)
- ☐ Partial (*in some cases, the proposed technology will replace the use of the comparator, but not in all cases*)
- ☐ Full (*subjects who receive the proposed intervention will not receive the comparator*)

Please outline and explain the extent to which the current comparator is expected to be substituted:

The proposed HRR testing strategy would be used in conjunction with current standard management of mCSPC and does not replace existing treatment approaches. Patients would continue to receive standard systemic therapies, including ADT, ARPI therapy and, where appropriate, docetaxel. The proposed testing strategy is intended to provide additional information to support treatment selection by identifying patients with HRR gene alterations.

Outcomes

(Please copy the below questions and complete for each outcome)

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): (please select your response)

- ☒ Health benefits
- ☒ Health harms
- ☒ Resources
- ☒ Value of knowing

Outcome description – please include information about whether a change in patient management, or prognosis, occurs as a result of the test information:

Patients with mCSPC who are identified as having HRR gene alterations may become eligible for biomarker-directed treatment that would not otherwise be available based on current clinical management. The test information therefore has the potential to change treatment selection by identifying a biomarker-defined subgroup of patients who may benefit from targeted therapy.

By enabling identification of patients with HRR gene alterations, the proposed testing strategy supports selection of patients consistent with those evaluated in the TALAPRO-3 study. Improved treatment selection has the potential to translate into improved clinical outcomes, including delayed disease progression, while supporting a precision medicine approach to the management of mCSPC.

Proposed MBS items

How is the technology/service funded at present? (for example: research funding; State-based funding; self-funded by patients; no funding or payments):

MBS funded. BRCA1/2 testing is currently funded under MBS items 73303 and 73304 for patients with mCRPC to determine eligibility for treatment under the PBS. This application seeks amendment of the existing MBS items to enable identification of HRR gene alterations in patients with mCSPC. The proposed amendment does not introduce a new testing methodology and would utilise existing laboratory infrastructure and testing pathways.

Please provide at least one proposed item with their descriptor and associated costs, for each population/Intervention: (please copy the below questions and complete for each proposed item)

MBS item number (where used as a template for the proposed item)	73303
Category number	6
Category description	PATHOLOGY SERVICES
Proposed item descriptor	A test of tumour tissue from a patient with metastatic <i>castration-sensitive prostate cancer</i> , including subsequent characterisation of germline gene variants should tumour tissue testing undertaken during the same service be inconclusive, requested by a specialist or consultant physician, to detect <i>homologous recombination repair (HRR) gene alterations (ATM, ATR, BRCA1, BRCA2, CDK12, CHEK2, FANCA, MLH1, MRE11A, NBN, PALB2 and RAD51C)</i> to determine eligibility for a relevant treatment under the Pharmaceutical Benefits Scheme. Applicable once per primary tumour diagnosis.
Proposed MBS fee	\$1,000
Indicate the overall cost per patient of providing the proposed health technology	\$1,000
Please specify any anticipated out of pocket expenses	\$250
Provide any further details and explain	Applicable once per lifetime Proposed additions are italicised in table. The change will not result in a change to testing methodology, the patient population who access testing through the MBS, or to the MBS fee

MBS item number (where used as a template for the proposed item)	73304
Category number	6
Category description	PATHOLOGY SERVICES
Proposed item descriptor	Detection of germline <i>homologous recombination repair (HRR) gene alterations (ATM, ATR, BRCA1, BRCA2, CDK12, CHEK2, FANCA, MLH1, MRE11A, NBN, PALB2 and RAD51C)</i> , in a patient with metastatic <i>castration-sensitive prostate cancer</i> , for whom testing of tumour tissue is not clinically feasible, requested by a specialist or consultant physician, to determine eligibility for a relevant treatment under the Pharmaceutical Benefits Scheme. Applicable once per lifetime.
Proposed MBS fee	\$1,000
Indicate the overall cost per patient of providing the proposed health technology	\$1,000
Please specify any anticipated out of pocket expenses	\$250
Provide any further details and explain	Applicable once per lifetime Proposed additions are italicised in table. The change will not result in a change to testing methodology, the patient population who access testing through the MBS, or to the MBS fee.

Algorithms

Preparation for using the health technology

Define and summarise the clinical management algorithm, including any required tests or healthcare resources, before patients would be eligible for the proposed health technology:

Patients with suspected prostate cancer typically undergo investigation with prostate-specific antigen (PSA) testing, digital rectal examination (DRE), multiparametric magnetic resonance imaging (mpMRI) and prostate biopsy to establish a diagnosis. Following diagnosis, imaging investigations such as computed tomography (CT), magnetic resonance imaging (MRI), bone scan and increasingly PSMA-PET may be used to determine disease stage and identify metastatic disease.

Patients diagnosed with mCSPC are generally managed by a specialist multidisciplinary team and commence standard systemic treatment, including androgen deprivation therapy (ADT), often in combination with an androgen receptor pathway inhibitor (ARPI), namely darolutamide, enzalutamide, apalutamide, and, where appropriate, docetaxel.

Prior to the proposed health technology, no MBS-funded HRR gene alteration testing is routinely performed in the mCSPC setting to inform treatment selection. Existing MBS items 73303 and 73304 support BRCA1/2 testing in patients with mCRPC; however, there is currently no equivalent MBS-funded testing pathway for HRR gene alterations in patients with mCSPC.

The healthcare resources used prior to the proposed health technology therefore include specialist consultations, pathology services, diagnostic imaging, biopsy procedures and standard systemic treatment for mCSPC.

Is there any expectation that the clinical management algorithm before the health technology is used will change due to the introduction of the proposed health technology?

No.

The proposed amendment is not expected to change the clinical management algorithm prior to use of the health technology. Patients with suspected or confirmed prostate cancer would continue to undergo standard diagnostic and staging investigations, including PSA testing, imaging and biopsy, followed by assessment and management according to current clinical practice. The proposed amendment does not introduce a new testing methodology, but rather extends the existing testing pathway to identify HRR gene alterations in patients with mCSPC using existing laboratory infrastructure and testing processes.

Describe and explain any differences in the clinical management algorithm prior to the use of the proposed health technology vs. the comparator health technology:

There are no material differences in the clinical management algorithm prior to use of the proposed health technology compared with the comparator. Patients would continue to undergo standard diagnostic, staging and treatment assessment processes for mCSPC. The proposed amendment does not alter the clinical pathway prior to testing and does not introduce additional diagnostic investigations before patients are considered for the proposed health technology.

Use of the health technology

Explain what other healthcare resources are used in conjunction with delivering the proposed health technology:

The proposed health technology would utilise the same healthcare resources currently used for genomic testing in prostate cancer. These include specialist consultations, pathology services, tumour tissue and/or blood sample collection, accredited molecular pathology laboratory testing, interpretation of results by appropriately qualified molecular pathologists, and communication of results to the treating specialist. The proposed amendment does not introduce additional healthcare resources beyond those currently used for genomic testing and delivery of existing MBS-funded BRCA1/2 testing services (73303 and 73304).

Explain what other healthcare resources are used in conjunction with the comparator health technology:

Current management without HRR gene alteration testing utilises standard healthcare resources for the management of mCSPC, including specialist consultations, pathology services, diagnostic imaging, biopsy procedures, androgen deprivation therapy (ADT), androgen receptor pathway inhibitor (ARPI) therapy and, where appropriate, docetaxel. No molecular testing is routinely performed to inform treatment selection in the mCSPC setting.

Describe and explain any differences in the healthcare resources used in conjunction with the proposed health technology vs. the comparator health technology:

The proposed health technology would utilise existing healthcare resources currently used for genomic testing in prostate cancer, including tumour tissue and/or blood sample collection, accredited molecular pathology laboratory testing, interpretation of results by appropriately qualified molecular pathologists and reporting of results to the treating specialist. Compared with the comparator, the proposed testing strategy introduces molecular testing for HRR gene alterations but does not require new testing methodologies, laboratory infrastructure or clinical referral pathways.

Clinical management after the use of health technology

Define and summarise the clinical management algorithm, including any required tests or healthcare resources, *after* the use of the proposed health technology:

Following testing, patients whose tumours are found to harbour HRR gene alterations may be considered for biomarker-directed treatment in accordance with relevant PBS eligibility criteria and contemporary clinical practice. The test result therefore informs treatment selection by identifying a biomarker-defined subgroup of patients who may be eligible for treatment under the PBS.

Patients whose tumours do not harbour HRR gene alterations would continue to be managed according to standard clinical practice for mCSPC, including androgen deprivation therapy (ADT), androgen receptor pathway inhibitor (ARPI) therapy and, where appropriate, docetaxel.

Following treatment selection, patients would continue to undergo routine monitoring and disease management, including specialist review, PSA testing, imaging investigations and assessment of treatment response in accordance with standard clinical practice. The proposed testing strategy does not alter ongoing monitoring requirements but provides additional information to support treatment selection on the PBS.

Define and summarise the clinical management algorithm, including any required tests or healthcare resources, *after* the use of the comparator health technology:

Under the comparator, patients with mCSPC are managed according to current clinical practice without HRR gene alteration testing. Treatment selection is based on clinical factors and disease characteristics rather than biomarker status, and typically includes androgen deprivation therapy (ADT), androgen receptor pathway inhibitor (ARPI) therapy and, where appropriate, docetaxel.

Patients continue to undergo routine disease monitoring, including specialist review, PSA testing, imaging investigations and assessment of treatment response in accordance with standard clinical practice. As no HRR testing is performed, treatment selection is not informed by HRR gene alteration status.

Describe and explain any differences in the healthcare resources used *after* the proposed health technology vs. the comparator health technology:

Compared with the comparator, the proposed health technology introduces molecular testing for HRR gene alterations and reporting of results to inform treatment selection. Patients whose tumours harbour HRR gene alterations may be identified for biomarker-directed treatment in accordance with relevant PBS eligibility criteria. Aside from the addition of HRR testing and associated pathology resources, ongoing disease management, monitoring and specialist care are expected to remain consistent with current clinical practice.

Insert diagrams demonstrating the clinical management algorithm with and without the proposed health technology:

Please ensure that the diagrams provided do not contain information under copyright.

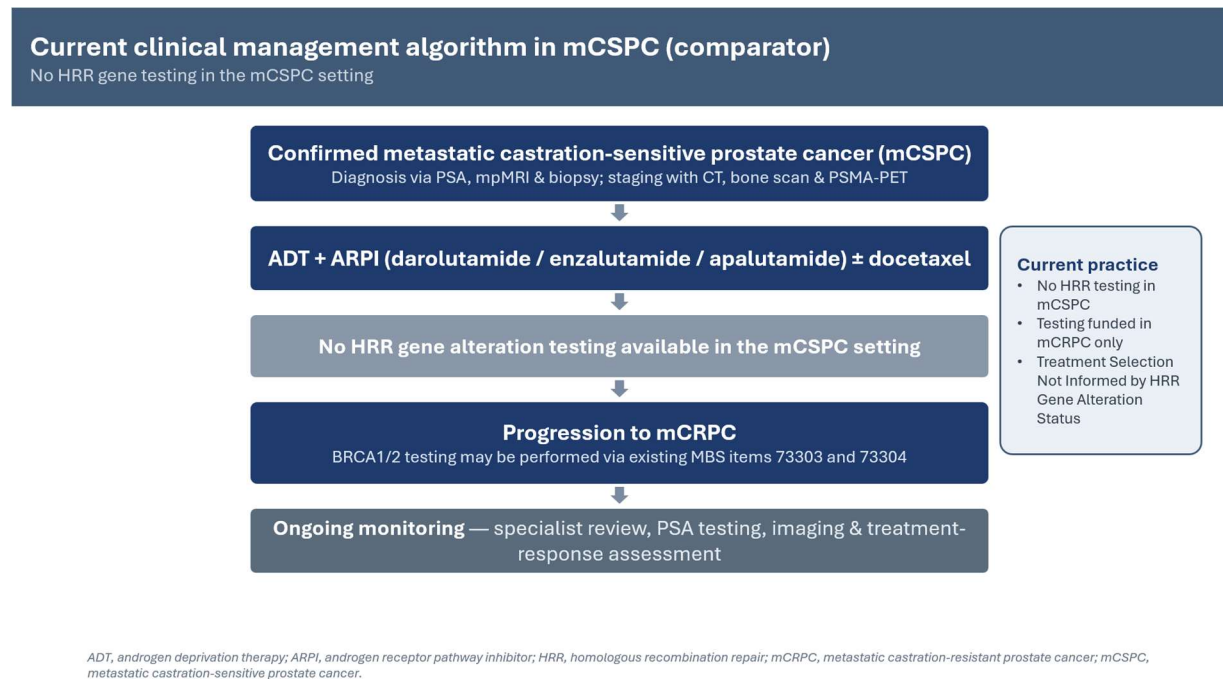


Figure 1 Current treatment algorithm

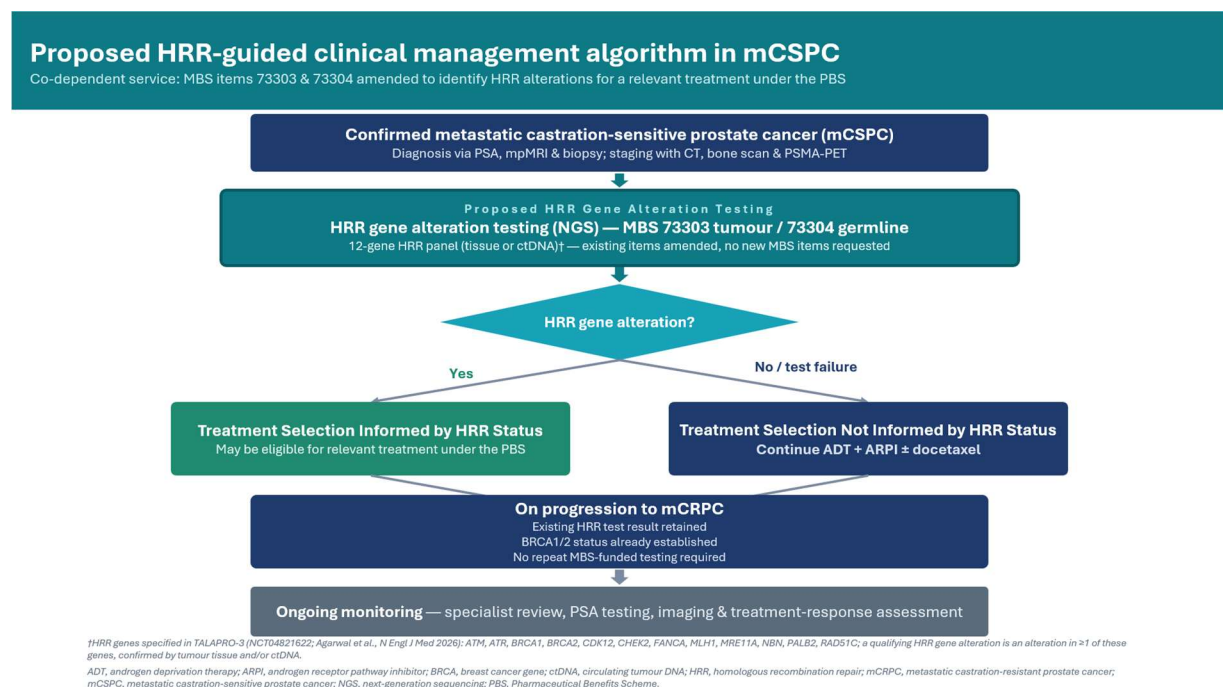


Figure 2 Proposed treatment algorithm

Claims

In terms of health outcomes (comparative benefits and harms), is the proposed technology claimed to be superior, non-inferior or inferior to the comparator(s)? (please select your response)

- ☒ Superior
☐ Non-inferior
☐ Inferior

Please state what the overall claim is, and provide a rationale:

Efficacy:

A claim of superior health outcomes is made for the proposed HRR testing strategy compared with current management without HRR testing. The proposed testing strategy enables identification of a biomarker-defined population whose treatment selection may be informed by HRR gene alteration status. In the Phase III TALAPRO-3 study, patients were prospectively identified using molecular testing and selected on the basis of HRR gene alteration status. By identifying patients consistent with those evaluated in TALAPRO-3, the proposed testing strategy has the potential to improve treatment selection and clinical outcomes compared with current practice, in which treatment selection is not informed by HRR gene alteration status.

The proposed HRR testing strategy is not expected to introduce additional clinically significant harms beyond those associated with current clinical practice and existing genomic testing pathways.

Why would the requestor seek to use the proposed investigative technology rather than the comparator(s)?

The proposed investigative technology enables identification of patients with mCSPC whose tumours harbour HRR gene alterations and therefore allows treatment selection to be informed by biomarker status. Under the comparator, patients are managed according to current clinical practice without HRR gene alteration testing, and treatment selection is not informed by HRR status.

In the Phase III TALAPRO-3 study, patients were prospectively identified using molecular testing and were required to harbour an alteration in at least one of 12 pre-specified HRR genes. The study therefore evaluated a biomarker-defined population selected on the basis of HRR gene alteration status. The proposed amendment seeks to identify the same HRR-altered population in clinical practice, supporting alignment between the population selected for treatment and the population in which the clinical benefits of treatment were demonstrated.

Identify how the proposed technology achieves the intended patient outcomes:

Genomic testing for HRR gene alterations in patients with mCSPC has the potential to improve patient outcomes by identifying a biomarker-defined population that may benefit from targeted treatment. Identification of HRR gene alterations informs treatment selection and enables identification of patients who may be eligible for relevant treatment under the PBS.

In the Phase III TALAPRO-3 study, patients were prospectively identified using molecular testing and were required to harbour an alteration in at least one of 12 pre-specified HRR genes. The study therefore evaluated a biomarker-defined population selected on the basis of HRR gene alteration status. The proposed testing strategy seeks to identify the same HRR-altered population in clinical

practice, supporting alignment between the population selected for treatment and the population in which the clinical benefits of treatment were demonstrated.

By enabling identification of patients with HRR gene alterations, the proposed testing strategy has the potential to improve treatment selection and patient outcomes while supporting a precision medicine approach to the management of mCSPC.

For some people, compared with the comparator(s), does the test information result in:

A change in clinical management? ☒ Yes

A change in health outcome? ☒ Yes

Other benefits? ☐ No

Please provide a rationale, and information on other benefits if relevant:

Patients with mCSPC who are identified as having HRR gene alterations may become eligible for biomarker-directed treatment that would not otherwise be available based on current clinical management. The test information therefore has the potential to change treatment selection by identifying a biomarker-defined subgroup of patients who may benefit from targeted therapy.

By enabling identification of patients with HRR gene alterations, the proposed testing strategy supports selection of patients consistent with those evaluated in the Phase III TALAPRO-3 study. Improved treatment selection has the potential to translate into improved clinical outcomes while supporting a precision medicine approach to the management of mCSPC.

In terms of the immediate costs of the proposed technology (and immediate cost consequences, such as procedural costs, testing costs etc.), is the proposed technology claimed to be more costly, the same cost or less costly than the comparator? (please select your response)

- ☒ More costly
☐ Same cost
☐ Less costly

Provide a brief rationale for the claim:

The proposed amendment extends molecular testing to identify HRR gene alterations in patients with mCSPC. While the proposed MBS fee is expected to remain aligned with existing MBS items 73303 and 73304 and no new testing methodology is introduced, the proposed testing strategy may result in additional testing costs relative to current clinical practice, in which HRR gene alteration testing is not routinely performed in the mCSPC setting.

Summary of Evidence

Provide one or more recent (published) high quality clinical studies that support use of the proposed health service/technology. At 'Application Form lodgement',

Do not attach full text articles; just provide a summary (repeat columns as required).

	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***
Pivotal study					
1	Randomised Phase III trial	TALAPRO-3: Talazoparib + Enzalutamide Compared with Placebo + Enzalutamide for the Treatment of Patients with mCSPC Harboring HRR Gene Alterations. Presented at: American Society of Clinical Oncology (ASCO) Annual Meeting; May–June 2026. Abstract LBA5007.	Phase III randomised study evaluating talazoparib plus enzalutamide versus placebo plus enzalutamide in patients with HRR gene-altered mCSPC. Patients were prospectively identified using molecular testing for alterations in one of 12 pre-specified HRR genes.	ASCO 2026: TALAPRO-3: Talazoparib + Enzalutamide Compared with Placebo + Enzalutamide for the Treatment of Patients with mCSPC Harboring HRR Gene Alterations	Agarwal 2026
2	Randomised Phase III trial	Talazoparib plus enzalutamide in men with first-line metastatic castration-resistant prostate cancer (TALAPRO-2): a randomised, placebo-controlled, phase 3 trial ClinicalTrials.gov NCT03395197	The purpose of this study is to evaluate the efficacy and safety (including evaluating side effects) of combination of talazoparib and enzalutamide versus placebo and enzalutamide in patients with metastatic castration-resistant prostate cancer (mCRPC)	https://pubmed.ncbi.nlm.nih.gov/37285865/	Agarwal et al 2023 Lancet. 2023 Jul 22;402(10398):291-303
Diagnostic studies					
3	Diagnostic study	Inherited DNA-repair gene mutations in men with metastatic prostate cancer	Multicentre study that recruited 692 men with metastatic prostate cancer who were unselected for family history of cancer or age at diagnosis. Germline DNA was isolated and used multiplex sequencing assays to assess mutations in 20 DNA-	https://www.nejm.org/doi/full/10.1056/NEJMoa1603144	Pritchard et al, 2016 N Engl J Med 2016; 375:443-453

	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***
			repair genes associated with autosomal dominant cancer-predisposition syndromes.		
4	Diagnostic study	BRCA Mutation Testing in Men With Metastatic Castration-Resistant Prostate Cancer: Practical Guidance for Australian Clinical Practice	Australian consensus guidance on molecular testing pathways to identify BRCA1/2 and other HRR alterations in mCRPC. Reports plasma ctDNA showed 81% positive and 92% negative agreement with tumour tissue for BRCA1, BRCA2 and ATM.	https://onlinelibrary.wiley.com/doi/10.1111/ajco.14150	Azad et al, 2025. Asia Pac J Clin Oncol. 2025
5	Diagnostic study	Homologous recombination repair genetic testing variables and diagnostic paths for prostate cancer patients: a multicenter cohort study	Multicentre cohort of 1400 prostate cancer patients undergoing germline, tumour and/or ctDNA HRR testing (2020-2025). (Likely) pathogenic HRR variants in 17.7%; concordance between tumour and ctDNA testing 83.9%; conclusive result rate 89.7%.	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC12921449/	Multicentre cohort, 2025. (PMC12921449)
6	Diagnostic study	Impact of homologous recombination repair/BRCA gene alterations on survival in a real-world setting of metastatic prostate cancer	Real-world analysis of the prognostic impact of HRR/BRCA gene alterations on survival outcomes in patients with metastatic prostate cancer.	https://onlinelibrary.wiley.com/doi/10.1111/bju.16462	Wenzel et al, 2025. BJU Int. 2025 Jan;135(1):117-124
7	Diagnostic study	Treatment patterns and outcomes in metastatic castration-resistant prostate cancer patients with and without somatic or germline alterations in homologous recombination repair genes	Real-world study of treatment patterns and outcomes in mCRPC patients stratified by presence of somatic or germline HRR gene alterations.	https://pubmed.ncbi.nlm.nih.gov/38417742/	Ann Oncol. 2024 May;35(5):458-472
Other studies					
8	Phase II trial	BRCAAWAY: A randomized phase 2 trial of abiraterone, olaparib, or abiraterone + olaparib in patients with metastatic castration-resistant prostate cancer (mCRPC) with DNA repair defects.	61 pts had NGS testing; 60 pts were randomized to Arms 1-3; to date 59 are evaluable for toxicity and 53 are evaluable for PFS. Mutational status: BRCA1 only n = 2, BRCA2 only n = 39, ATM only n = 8, and > 1 HRRm n = 11. 34 pts had germline and 26 had somatic mutations. In mCRPC pts with inactivating BRCA1, BRCA2 and/or ATM alterations Abi/pred +	https://ascopubs.org/doi/10.1200/JCO.2022.40.16_suppl.5018	Hussain et al, 2022 ASCO 2022 Conference abstract

	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***
		Clinical trial information: NCT03012321	olaparib was well tolerated and resulted in longer PFS and better PSA response vs either agent alone.		
9	Randomised Phase III trial	PARP and androgen-signaling inhibition plus ADT in metastatic prostate cancer (TALAPRO-3). ClinicalTrials.gov NCT04821622	Phase 3 trial of talazoparib + enzalutamide vs placebo + enzalutamide plus ADT in 599 patients with HRR gene-altered metastatic castration-sensitive prostate cancer. rPFS significantly improved (median not reached vs 45.8 months; HR 0.48); OS immature.	https://www.nejm.org/doi/10.1056/NEJMoa2604126	Agarwal et al, 2026. N Engl J Med. 2026
Reviews					
10	Review	Targeting the DNA damage response: PARP inhibitors and new perspectives in the landscape of cancer treatment	Summary of the main DDR pathways, explain the current role of PARP inhibitors in cancer therapy and illustrate new therapeutic strategies targeting the DDR, focusing on the combinations of PARP inhibitors with other agents and on cell-cycle checkpoint inhibitors.	https://pubmed.ncbi.nlm.nih.gov/34800653/	Genta et al 2021 Crit Rev Oncol Hematol. 2021 Dec;168:103539
11	Review	DNA repair defects in prostate cancer: impact for screening, prognostication and treatment	Review covers the relationship between DNA repair defects and prostate cancer, highlighting the prevalence of mutations in key genes and their controversial association with clinical outcomes.	https://www.ncbi.nlm.nih.gov/pubmed/30281887/	Warner et al, 2019 BJU Int. 2019 May;123(5):769-776
12	Review	The emerging role of PARP inhibitors in prostate cancer: A narrative review	Narrative review of PARP inhibitor monotherapy and combination with androgen receptor pathway inhibitors across prostate cancer settings, including TALAPRO-2 rPFS and OS data and gene-by-gene benefit.	https://www.cancertreatmentreviews.com/article/S0305-7372(25)00122-7/fulltext	Cancer Treat Rev. 2025

	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***
13	Review	Integrating PARP inhibitors in mCRPC therapy: current strategies and emerging trends (talazoparib plus enzalutamide as first-line treatment)	Review of efficacy and safety of PARPi plus ARSI across all phase 3 RCTs in mCRPC, with focus on talazoparib + enzalutamide and strategies for patient selection.	https://www.dovepress.com/integrating-parp-inhibitors-in-mcrpc-therapy-current-strategies-and-em-peer-reviewed-fulltext-article-CMAR	Cancer Manag Res. 2024
14	Systematic review / meta-analysis	PARP inhibitor-based treatment in metastatic, castration-resistant prostate cancer (mCRPC): A systematic review and meta-analysis	Systematic review and meta-analysis of RCTs of PARP inhibitors alone or combined with androgen receptor-targeted agents in mCRPC, showing benefit especially in rPFS and in HRR+/BRCA1/2 populations.	https://bjui-journals.onlinelibrary.wiley.com/doi/full/10.1002/bco2.455	Roberto et al, 2025. BJUI Compass. 2025
15	Systematic review / umbrella review	Efficacy and safety of PARP inhibitors in prostate cancer: An umbrella review of systematic reviews and meta-analyses	Umbrella review of systematic reviews and meta-analyses; olaparib, talazoparib and rucaparib showed the strongest OS and PFS benefit, with combination PARPi + hormonal therapy most effective in BRCA1/2-mutant and HRR-deficient mCRPC.	https://www.sciencedirect.com/science/article/abs/pii/S1040842824003524	Crit Rev Oncol Hematol / Microbiol. 2025

* 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. For yet to be published research, provide high level information including population numbers and whether patients are being recruited or in post-recruitment.

*** If the publication is a follow-up to an initial publication, please advise. For yet to be published research, include the date of when results will be made available (to the best of your knowledge).

Identify yet-to-be-published 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 (repeat columns as required).

	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.	Randomised Phase III trial	Talapros-3: A phase 3, double-blind, randomized study of enzalutamide (ENZA) plus talazoparib (TALA) versus placebo plus enza in patients with DDR gene mutated metastatic castration-sensitive prostate cancer (mCSPC). ClinicalTrials.gov NCT04821622	The purpose of this study is to evaluate the efficacy and safety (including evaluating side effects) of combination of talazoparib and enzalutamide versus placebo and enzalutamide in patients with metastatic castration-resistant prostate cancer (mCRPC) with DDR gene mutations	Study of Talazoparib With Enzalutamide in Men With DDR Gene Mutated mCSPC - Full Text View - ClinicalTrials.gov	2026

* 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. For yet to be published research, provide high level information including population numbers and whether patients are being recruited or in post-recruitment.

*** If the publication is a follow-up to an initial publication, please advise. For yet to be published research, include the date of when results will be made available (to the best of your knowledge).

References

- Abida, A, Armenia, J et al, Gopalan, A et al. (2017). Prospective Genomic Profiling of Prostate Cancer Across Disease States Reveals Germline and Somatic Alterations That May Affect Clinical Decision Making JCO Precis Oncol. 2017; 1: PO.17.00029. doi: 10.1200/PO.17.00029.
- Armenia, J, Wankowicz, S, Liu, D, et al. (2018). The long tail of oncogenic drivers in prostate cancer. Nat Genet. 2018 May;50(5):645-651. doi: 10.1038/s41588-018-0078-z
- Chung, J; Dewal, N; Sokol, E, et al. (2019). Prospective Comprehensive Genomic Profiling of Primary and Metastatic Prostate Tumors. JCO Precision Oncology. DOI <https://doi.org/10.1200/PO.18.00283>
- Gandaglia, G., Karakiewicz, P. I., Briganti, A., Passoni, N. M., Schiffmann, J., Trudeau, V., . . . Sun, M. (2015). Impact of the Site of Metastases on Survival in Patients with Metastatic Prostate Cancer. European Urology, 68(2), 325-334. doi:10.1016/j.eururo.2014.07.020
- Kirby, M., Hirst, C., & Crawford, E. D. (2011). Characterising the castration-resistant prostate cancer population: a systematic review. Int J Clin Pract, 65(11), 1180-1192. doi:10.1111/j.1742-1241.2011.02799.x
- Parker, C., Castro, E., Fizazi, K., Heidenreich, A., Ost, P., Procopio, G., .clinicalguidelines@esmo.org, E. G. C. E. a. (2020). Prostate cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol, 31(9), 1119-1134. doi:10.1016/j.annonc.2020.06.011
-