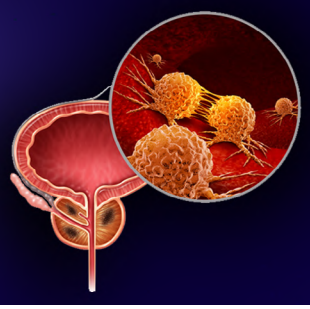
Prostate Cancer Practice Review™



Making Education Easy

Issue 30 - 2025

In this issue:

Abbreviations used in this issue:

^{177}Lu-PSMA-617 = lutetium-177-PSMA-617;
ADT = androgen-deprivation therapy;
ARPI = androgen receptor pathway inhibitor;
ASCO = American Society of Clinical Oncology;
AUA = American Urological Association; ***BRCA*** = BReast CAncer gene;
CT = computed tomography; **EMA** = European Medicines Agency;
ESMO = European Society for Medical Oncology;
FDA = US Food & Drug Administration; **HRR** = homologous recombinant repair;
MBS = Medicare Benefits Schedule;
mCSPC = metastatic castration-sensitive prostate cancer;
mCRPC = metastatic castration-resistant prostate cancer;
NICE = UK's National Institute for Health and Care Excellence;
PARP = poly(ADP-ribose) polymerase; **PBS** = Pharmaceutical Benefits Scheme;
PET = positron emission tomography; **PSA** = prostate-specific antigen;
PSMA = prostate-specific membrane antigen;
TGA = Therapeutic Goods Administration.

Welcome to the 30th issue of Prostate Cancer Practice Review.

This Review covers news and issues relevant to clinical practice in prostate cancer. It will bring you the latest updates, both locally and from around the globe, in relation to topics such as new and updated treatment guidelines, changes to medicines reimbursement and licensing, educational, professional body news and more. Finally, on the back cover you will find a summary of upcoming local and international educational opportunities including workshops, webinars and conferences.

We hope you enjoy this Research Review publication and look forward to hearing your comments and feedback.

Kind Regards,

Dr Janette Tenne
Editor
janette.tenne@researchreview.com.au

Clinical Practice

Advancing diagnostic excellence and health equity: The role of PSA screening in early detection of prostate cancer

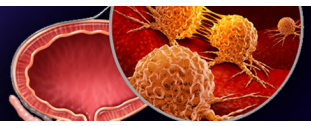
As part of the American Urological Association's (AUA's) enterprise to create and circulate publications promoting diagnostic excellence in urology to ultimately not only improve accurate determination of disease cause and prognosis and inform the appropriate treatment paradigm, but also optimise patient outcomes, an educational article on the role of prostate-specific antigen (PSA) screening in early detection of prostate cancer has been formulated. Designed primarily for urologists and primary care physicians in the US, the review is based on the 2023 update to the AUA's guideline on prostate cancer early detection and emphasises equitable care by highlighting the incommensurate prevalence of prostate cancer, with later diagnosis and significantly greater mortality, in Black men. The review comprises three parts – an easy-to-follow Clinical Decision Support tool with a flowchart/algorithm to guide initiation of risk-stratified PSA-based screening, an infographic educational tool to illustrate prostate cancer disparities and, a synopsis of the benefits and risks to screening.

The development of the review was enabled by a grant program administered through the Council of Medical Specialty Societies and is supported by a podcast (Episode 244 of the AUA Inside Tract podcast – available here and on iTunes).

The full resource, and other relevant publications for physicians treating patients with prostate cancer, can be downloaded from AUA's Diagnostic Excellence webpage

Earn CPD

Nursing and Midwifery Board of Australia (NMBA) Journal reading and watching videos (including Research Reviews') may be considered a self-directed activity set out in the NMBA Registration Standard: Continuing Professional Development. One hour of active learning will equal one hour of CPD. Details at NMBA CPD page.



Systemic therapy in patients with metastatic castration-resistant prostate cancer: ASCO guideline update

The American Society of Clinical Oncology (ASCO) have recently updated their clinical practice guidelines pertaining to systemic therapy in patients with metastatic castration-resistant prostate cancer (mCRPC). This is the first full update to these guidelines since their inception more than a decade ago, although rapid updates were published in 2022 and 2023 to include data on the radioligand therapy lutetium-177–labelled prostate-specific membrane antigen (PSMA)-617 (^{177}Lu-PSMA). Developed by an expert multidisciplinary panel, the document provides evidence-based recommendations for oncologists, primary care physicians, nuclear medicine clinicians and other health professionals. A rigorous systematic review of over 140 phase 2 and 3 randomised clinical trials published up to June 16, 2021 was first undertaken via the 'living' interactive evidence synthesis framework, and the resultant guidelines were ultimately informed by meta-analyses (random-effects DerSimonian-Laird and fixed-effect modelling) of data from 22 trials including almost 15,000 patients of androgen receptor pathway inhibitors (ARPIs; e.g., abiraterone), poly(ADP-ribose) polymerase (PARP) inhibitors, chemotherapy, and the cell-based immunotherapy sipuleucel-T. The resultant evidence-based draft recommendations have also undergone review and revision following public consultation.

In brief, the guidelines advise that therapy decisions in this space should be based on prior treatment received in the castration-sensitive or non-metastatic castration-resistant disease setting with personalisation for clinical status, symptom severity, therapy-related toxicity and cost, and emphasise the importance of somatic and germline genetic testing for BReast CAncer gene (*BRCA*) and other homologous recombinant repair (HRR) deficiencies prior to initiation of systemic therapy to determine the optimal therapeutic approach. Advocacy is also given for indefinite androgen-deprivation therapy (ADT; or surgical castration) and early integration of palliative and supportive care teams for symptom management for all patients with mCRPC, and for inclusion of bone-protective agents like denosumab or zoledronic acid in the treatment regimen for patients with bone metastases. Finally, the paucity of high-quality data on which to base advice regarding the optimal sequencing of therapies is noted, especially as more therapies move into the castration-sensitive treatment space.

The following treatment algorithm summarises the recommended treatment options for patients with mCRPC according to prior therapy.

	Previous treatment		
	ADT ± docetaxel	**ADT + ARPI**	**ADT + ARPI and docetaxel**
BRCA1/2-positive	• Talazoparib + enzalutamide • Olaparib + abiraterone • Niraparib + abiraterone	Olaparib monotherapy	Olaparib## monotherapy
Non-*BRCA* HRR-positive*	Talazoparib + enzalutamide	Olaparib monotherapy	Olaparib monotherapy
HRR-negative	• Abiraterone with prednisone • Enzalutamide • Docetaxel (only if not used in previous therapy)	• Docetaxel^ • Radium 223 • Cabazitaxel • Pembrolizumab (if MSI-H/dMMR)	
PSMA-positive			• ^{177}Lu-PSMA • Cabazitaxel
PSMA-negative + HRR-negative			• Cabazitaxel • Radium 223 • Pembrolizumab (if MSI-H/dMMR)
Special situations			
Oligometastatic disease/progression	Metastasis-directed therapy with radiation or surgery		
Indolent disease**	Sipuleucel-T		
Symptomatic bone-only disease#	Radium 223		
MSI-H/dMMR	Pembrolizumab		

* Aberrations in *PALB2*, *ATM*, *ATR*, *CHEK2*, *FANCA*, *RAD51C*, *NBN*, *MLH1*, *MRE11A* or *CDK12*

**Slow rising PSA, asymptomatic or low-volume disease without visceral metastases

Without known visceral metastases or large nodal (>3 cm in short axis) metastatic disease. Avoid concomitant use with abiraterone + prednisone

Rucaparib may be a suitable alternative for select patients

^ Cabazitaxel may be considered for selected patients if they have an allergic reaction or toxicity like peripheral neuropathy which precludes the use of docetaxel

dMMR = mismatch repair-deficient; **MSI-H** = microsatellite instability-high.

For patients with *de novo* or treatment-emergent small cell neuroendocrine carcinoma of the prostate the guidelines strongly advise first-line treatment with cisplatin or carboplatin plus etoposide followed by clinical trial enrolment in cases of progression. Carboplatin plus cabazitaxel is suggested for patients with pathogenic aberrations in at least two of the *TP53*, *RB1* and *PTEN* genes. A conditional recommendation suggests that select patients with small cell neuroendocrine carcinoma of the prostate may be suitable for immunotherapy plus chemotherapy, lurbinectedin, topotecan or tarlatamab, with the caveat that prospective studies supporting these agents in this population are lacking.

Finally, with regard to evaluating response to systemic therapy, radiologic assessment with technetium-99m (Tc99) bone scan and computed tomography (CT) scan of the chest, abdomen, and pelvis, in combination with blood tests including PSA, a complete blood count and comprehensive metabolic panel, plus clinical assessment, are advocated for. The routine use of PSMA positron emission tomography (PET)/CT for response assessment is not advised and this imaging modality should be restricted to identify patients with PSMA-expressing tumours suitable for ^{177}Lu-PSMA-617 therapy or to stage patients with a rising PSA in whom progression cannot be visualised on conventional imaging.

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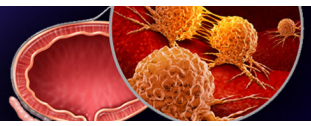
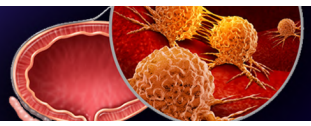




NICE prostate cancer resources in development

The UK's National Institute for Health and Care Excellence (NICE) are currently putting together several technology appraisal guidance documents relevant to physicians involved in the diagnosis or care of men with prostate cancer.

Some resources will be available later this year including:

- Darolutamide with ADT for treating metastatic castration-sensitive prostate cancer (mCSPC)
- Talazoparib with enzalutamide for untreated hormone-relapsed metastatic prostate cancer
- Abiraterone (originator and generics) for treating newly diagnosed high-risk mCSPC

Resources expected to be released in 2026/7, or later, include:

- Radium-223 dichloride with enzalutamide for treating asymptomatic or mildly symptomatic hormone-relapsed metastatic prostate cancer with bone metastases
- Rucaparib for treating hormone-relapsed metastatic prostate cancer with HRR deficiency after one therapy
- Apalutamide with gonadotrophin-releasing hormone agonist and radiotherapy for treating high-risk, localised or locally advanced prostate cancer
- Pembrolizumab with enzalutamide and ADT for treating mCSPC
- Apalutamide with radical prostatectomy for untreated high-risk, localised or locally advanced prostate cancer
- Talazoparib with enzalutamide for untreated mCSPC with a HRR mutation
- Capivasertib with abiraterone for treating mCSPC with *PTEN* deficiency
- Lutetium with ADT and receptor pathway inhibitors for treating PSMA-positive mCSPC

More information about these planned and in development resources is available on the NICE website

Regulatory News

TGA

New registrations

The Australian Therapeutic Goods Administration (TGA) have recently approved several novel abiraterone products relevant to clinicians treating patients with prostate cancer.

Two new abiraterone plus prednisolone tablet composite blister pack products - Andriga-10® and Andriga-5® (abiraterone acetate 500 mg plus prednisolone 5 mg; Actor Pharmaceuticals Pty Ltd; ARTG ID 437511 & ARTG ID 437512) – were added to the Australian Register of Therapeutic Goods (ARTG) in July, providing an alternative brand to Yonsa® MPRED (Sun Pharma ANZ). Both products come in two pack sizes - Andriga-10® with either 112 or 56 tablets of each medication and Andriga-5® with 112 or 56 tablets of 500 mg abiraterone acetate plus half the number of 5 mg prednisolone tablets (i.e., 56 or 28). Andriga-10® is indicated for newly diagnosed high-risk mCSPC in combination with ADT. Andriga-5® is indicated for the later-line treatment of mCRPC in asymptomatic or mildly asymptomatic patients after failure of ADT or taxane-based chemotherapy.

Several novel generic abiraterone acetate products from Cipla Australia and Glenmark Pharmaceuticals have been recently TGA approved, providing options for patients with prostate cancer beyond the innovator brand Zytiga® (Janssen-Cilag) and other previously approved generics (e.g., Abiraterone-Teva and Abiraterone Sandoz). The following products come in 250 mg and 500 mg strengths and are available in bottles and blister packs, respectively.

Cipla Australia

- Cip abiraterone (ARTG ID 444830 & ARTG ID 443940)
- Cipla abiraterone (ARTG ID 444831 & ARTG ID 443941)
- Xbira abiraterone (ARTG ID 444832 & ARTG ID 446770)

Glenmark Pharmaceuticals Australia

- Abiraterone Viatris (ARTG ID 453790 & ARTG ID 453789)
- Arabitro abiraterone (ARTG ID 489666 & ARTG ID 457885)

These new abiraterone products have not yet been evaluated by the Pharmaceutical Benefits Advisory Committee (PBAC) for Pharmaceutical Benefits Scheme (PBS) listing.

More information can be found on the TGA's Prescription medicines registration database.

July amendments to the MBS

New MBS items: theranostics for mCRPC

Following positive Medical Services Advisory Committee (MSAC) recommendation early last year for government subsidy of ^{177}Lu-PSMA radioligand therapy (and associated diagnostic PSMA-PET/CT imaging) for patients with progressive PSMA-positive mCRPC after standard therapeutic options, new Medicare Benefits Schedule (MBS) items are now in effect. These listings reduce the cost of imaging to ascertain suitability for ^{177}Lu-PSMA therapy in men with progressive disease after at least one ARPI and taxane-based chemotherapy and, in patients with demonstrated PSMA-positive disease, up to six treatment cycles of ^{177}Lu-PSMA therapy. Continuing Medicare-subsidised therapy after the initial two cycles is restricted to responding patients without disease progression. While these services provide some financial support for patients to access this potentially life-saving therapy, patients may be still liable for significant costs. Additional Medicare claims can be made for upfront out-of-pocket costs exceeding $10,000 by submitting form MS014 either by mail to Medicare or in-person at a Services Australia service centre.

To date ^{177}Lu vipivotide tetraxetan (Pluvicto™; 1000 Megabecquerel [MBq] /mL solution; Novartis Pharmaceuticals Australia Pty Limited) is the only therapeutic radiopharmaceutical TGA approved for the later-line treatment of adult patients with progressive PSMA-positive mCRPC after ARPI and taxane-based chemotherapy (ARTG ID 410282; Australian Prescription Medicine Decision Summary), but these novel MBS items are therapy-type agnostic and will cover any ^{177}Lu-PSMA theranostics approved in the future.

The novel MBS items for theranostics in men with prostate cancer are:

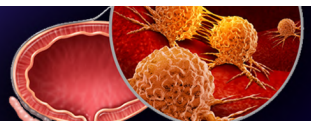
MBS ITEM NUMBER AND DESCRIPTION		FEE	BENEFIT	
			75%	**85%**
61528	Whole body PSMA PET imaging to determine eligibility for 177Lu-PSMA therapy	$1,300	$975.00	$1,197.60
16050	Up to two initial treatment cycles of 177Lu-PSMA therapy plus whole-body Lu-PSMA SPECT	$8,000	$6,000.00	$7,897.60
16055	Up to four cycles of 177Lu-PSMA therapy in the continuing treatment phase plus whole-body Lu-PSMA SPECT	$8,000	$6,000.00	$7,897.60

The full item descriptions can be found on the MBS Online website.

Earn CPD

Royal Australasian College of Physicians (RACP) MyCPD participants can claim the time spent reading and evaluating research reviews as CPD in the online MyCPD program. Please contact MyCPD@racp.edu.au for any assistance.

Royal Australian & New Zealand College of Radiologists (RANZCR) members can claim reading related to their practice as a CPD activity under the category 'journal reading and web based no certificate *reflection required'. More info.



Outcome on MBS item for focal irreversible electroporation pending

An application from Getz Healthcare for an MBS item for focal irreversible electroporation for prostate tumour tissue in patients with prostate cancer (1794) was considered at the PICO Advisory Subcommittee (PASC) meeting in April but the outcome has not been released. Per the application, this ablative technique is intended as a function preserving alternative to prostatectomy or radiation therapy in patients with low- to intermediate-grade non-metastatic prostate cancer, or as a salvage therapy for patients with localised disease recurrence after radiation therapy that is not amenable to surgical resection. The NanoKnife system employs electrical pulses to kill soft tissue tumours and is guided by transrectal ultrasound. An MBS fee of $1,815.35 has been proposed.

All application documents can be found on the MSAC webpage

Annual indexation factor

The Australian Government's Department of Health, Disability & Ageing have announced that the MBS indexation factor for 1st July 2025 is 2.4%.

This annual indexation increase is applicable to most general medical services items and diagnostic imaging services (except positron emission tomography and nuclear medicine modifier items), as well as pathology items in Groups P1 – P6, P8 and P12.

Changes to management of chronic conditions & general medical services

Chronic condition management arrangements under the MBS are being streamlined, and there are updates to MBS funded general medical services, effective from July.

Salient changes include:

- Amalgamation of the existing two-plan framework consisting of a GP management plan plus team care arrangements into a single planning item (GP chronic condition management plan)
- Standardising fees for the development and review of chronic condition management plans
- Creation of novel telehealth attendance items for the development and review of GP chronic condition management plans
- Overhaul of referral requirements for specified allied health services

For patients with chronic conditions and pre-existing GP plus team care arrangements a one-year transition period is provided to move to the new system.

Pertinent changes to general medical services include:

- Novel MBS items for telehealth appointments with specialist and consultant physicians
- Removal of MBS items specific for COVID-19 vaccine suitability evaluation

More information is available here

News in Brief

FDA approves a new indication for darolutamide in mCSPC

The US Food & Drug Administration (FDA) recently expanded approved prostate cancer indications for darolutamide (Nubeqa®, Bayer Healthcare Pharmaceuticals Inc.) to include the treatment of mCSPC without concomitant chemotherapy. Previous indications included mCSPC in combination with docetaxel, as well as non-metastatic castration-resistant disease. Approval was based on demonstration of a significant delay in disease progression with daroluatmide versus placebo in the ARANOTE trial. Patients in both trial arms received a concomitant gonadotropin-releasing hormone analogue, or had undergone bilateral orchiectomy. Evaluation of this novel indication for darolutamide was done through the international Project Orbis framework in collaboration with the TGA and regulatory bodies from Canda, Switzerland and the UK but, to date, it has not been approved outside the US.

The press release from the FDA can be read here. Full prescribing information for darolutamide in the US is available at Drugs@FDA.

EMA warns of risk of suicidal thoughts with finasteride and dutasteride medicines

The European Medicines Agency (EMA) has warned that suicidal ideation is a rare but possible adverse effect with finasteride - and potentially dutasteride - tablets, medications used to treat androgenetic alopecia and benign prostatic hyperplasia. To alert consumers and mitigate risk they have updated the relevant product information to advise that patients who experience issues with sexual function that may contribute to mood alterations seek medical advice, and included a patient card in medication packaging. EMA's safety committee have stated that the benefits of these medications for approved uses still outweigh their risks.

More information is available here

Carotuximab combo safe in mCRPC

Preliminary data from the first ten patients with mCRPC treated with carotuximab in a US open-label phase 2 trial show a favourable safety profile for the first-in-class CD105 antagonist. According to a press release from the trial sponsor no dose-limiting toxicities or severe (grade 3/4) adverse events were observed with a doublet regimen of carotuximab plus apalutamide in patients with mCRPC that progressed on androgen receptor signalling inhibitor therapy. Carotuximab's clinical potential will continue to be evaluated in the trial, with interim efficacy results expected in September but researchers hope that by offering a novel mechanism to overcome resistance to conventional hormone-based therapies it may be an efficacious treatment for patients with limited options.

The full press release can be found here

ESMO Asia Congress 2025

The 2025 European Society for Medical Oncology (ESMO) Asia Congress will be held in Singapore in December.

Registered participants will have access to scientific and educational sessions as well as poster presentations, networking opportunities, participation in the Industry Satellite Symposia and access to online resources though OncologyPRO.

Early registration closes 3 September 2025. Register here

Conferences, Workshops, and CPD

Please click on the links below for upcoming local and international prostate cancer meetings, workshops and CPD.

AUA - Meetings & Education
COSA – Events
MOGA – Events
USANZ – Events

Research Review Publications

Genitourinary Cancer Research Review with Associate Professor Andrew Weickhardt

Prostate Cancer Research Review with Professor Niall Corcoran

Urology Research Review with Professor Eric Chung