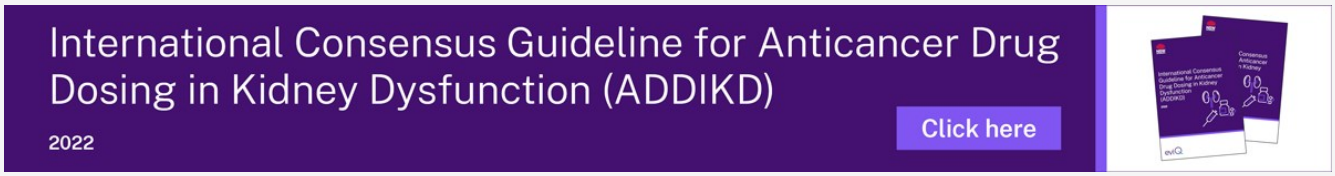
# Prostate metastatic castration-resistant abiraterone and prednisolone

**ID: 1417** v.4 **Endorsed** Essential Medicine List

Check for clinical trials in this patient group. Link to Australian Clinical Trials website

The anticancer drug(s) in this protocol may have been included in the ADDIKD guideline. Dose recommendations in kidney dysfunction have yet to be updated to align with the ADDIKD guideline. Recommendations will be updated once the individual protocol has been evaluated by the reference committee. For further information refer to the ADDIKD guideline. To assist with calculations, use the eviQ Estimated Glomerular Filtration Rate (eGFR) calculator.




**Related pages:**

- Prostate metastatic zoledronic acid
- Prostate metastatic denosumab
- Androgen deprivation therapy (ADT) for prostate cancer
- Prostate metastatic castration-sensitive abiraterone and prednisolone

## Treatment schedule - Overview

| Drug | Dose | Route |
|---|---|---|
| Abiraterone | 1,000 mg ONCE a day * | PO |
| Prednisolone ** | 10 mg ONCE a day | PO |

* 4 x 250 mg or 2 x 500 mg tablets

** prednisolone can be given as 5 mg TWICE a day. It is given continuously during all cycles of treatment. This is often tapered off slowly over a period of 1 month after completion of abiraterone at the discretion of the medical officer.

**Continuous until disease progression or unacceptable toxicity**

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**Notes:**
Dexamethasone 0.5 mg daily may be used as an alternative to prednisolone. A phase 2 trial demonstrated an increase in PSA response rate with dexamethasone.

Patients who were receiving a luteinising hormone-releasing hormone (LHRH) agonist prior to starting abiraterone should continue to receive a LHRH agonist.

Bone modifying agents (e.g. zoledronic acid, denosumab) should be considered in patients with recurrent metastatic prostate cancer since it may prevent skeletal-related events and improve bone mineral density.[1]

**Drug status:** **Abiraterone** is PBS authority

Abiraterone is available as **250 mg** and **500 mg** tablets

**Cost:** ~ $3,080 per month

## Treatment schedule - Detail

*The supportive therapies (e.g. antiemetics, premedications, etc.), infusion times, diluents, volumes and routes of administration, if included, are listed as defaults. They may vary between institutions and can be substituted to reflect individual institutional policy.*

*Antiemetics if included in the treatment schedule are based upon recommendations from national and international guidelines. These are **defaults only** and may be substituted to reflect individual institutional policy. Select here for recommended doses of alternative antiemetics.*

| Continuous treatment | | |
|---|---|---|
| Abiraterone | 1,000 mg (PO) | ONCE a day (4 x 250 mg or 2 x 500 mg tablets) on an empty stomach one hour before food or two hours after food. CAUTION: DO NOT take with food as this increases serum drug levels and side effects. |
| Prednisolone | 10 mg (PO) | ONCE a day with or after food. Can be given as 5mg TWICE a day |

**Continuous until disease progression or unacceptable toxicity**

## Indications and patient population

- Metastatic castration-resistant prostate cancer
- ECOG performance status 0 to 2.

## Clinical information

| | |
|---|---|
| **Caution with oral anti-cancer drugs** | Select links for information on the safe prescribing, dispensing and administration of orally administered anti-cancer drugs.<br>Read more about the COSA guidelines and oral anti-cancer therapy |
| **Emetogenicity minimal or low** | No routine prophylaxis required. If patients experience nausea and/or vomiting, consider using the low emetogenic risk regimen.<br>Read more about preventing anti-cancer therapy induced nausea and vomiting |
| **Corticosteroids** | Diabetic patients should monitor their blood glucose levels closely. To minimise gastric irritation, advise patient to take immediately after food. Consider the use of a H2 antagonist or proton pump inhibitor if appropriate.<br>Read more about acute short term effects from corticosteroids |
| **Hypertension, hypokalaemia and fluid retention** | Abiraterone may increase mineralocorticoid levels resulting in hypertension, hypokalaemia and fluid retention. Correct pre-existing hypertension and hypokalaemia prior to commencing treatment.<br>Monitor blood pressure, potassium levels and for fluid retention at least once a month and treat if required. In severe or persistent hypertension, permanent discontinuation should be considered.<br>Administration of prednisolone in this protocol reduces the incidence of these side effects. |
| **Hepatotoxicity** | Hepatotoxicity has been observed with this treatment. Onset of hepatic dysfunction typically occurs within 3 months of starting treatment.<br>Monitor for abnormal liver function tests (LFTs), jaundice and tiredness. Refer to blood tests and dose modification sections for specific recommendations. |
| **Bone modifying agents** | The use of a bone modifying agent (BMA) should be considered as it may prevent skeletal related events and improve bone mineral density. Bone modifying agents include bisphosphonates (e.g. zoledronic acid and pamidronate) and the monoclonal antibody denosumab. |

| | |
|---|---|
| **Blood tests** | FBC, EUC, LFTs and BSL at baseline then repeat monthly or as clinically indicated. Repeat LFTs every 2 weeks for the first 3 months of treatment and then monthly. PSA as clinically indicated. |
| **Vaccinations** | Live vaccines are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease.<br>Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the Australian Immunisation Handbook.<br>Read more about COVID-19 vaccines and cancer. |
| **Fertility and fathering a child** | Cancer treatment can have harmful effects on fertility and this should be discussed with all patients of reproductive potential prior to commencing treatment. It is important that all patients of reproductive potential use effective contraception whilst on therapy and after treatment finishes. Effective contraception methods and contraception timeframe should be discussed with all patients of reproductive potential.<br>Read more about the effect of cancer treatment on fertility |

## Dose modifications

*Evidence for dose modifications is limited, and the recommendations made on eviQ are intended as a guide only. They are generally conservative with an emphasis on safety. Any dose modification should be based on clinical judgement, and the individual patient's situation including but not limited to treatment intent (curative vs palliative), the anti-cancer regimen (single versus combination therapy versus chemotherapy versus immunotherapy), biology of the cancer (site, size, mutations, metastases), other treatment related side effects, additional co-morbidities, performance status and patient preferences.Suggested dose modifications are based on clinical trial findings, product information, published guidelines and reference committee consensus . The dose reduction applies to each individual dose and not to the total number of days or duration of treatment cycle unless stated otherwise. Non-haematological gradings are based on Common Terminology Criteria for Adverse Events (CTCAE) unless otherwise specified. Renal and hepatic dose modifications have been standardised where possible. For more information see dosing considerations & disclaimer .*

The dose recommendations in kidney dysfunction (i.e.renal impairment) displayed may not reflect those in the ADDIKD guideline and have been included for historical reference only. Recommendations will be updated once the individual protocol has been evaluated by the reference committee, with this version of the protocol then being archived. Clinicians are expected to refer to the ADDIKD guideline prior to prescribing in kidney dysfunction.
**International Consensus Guideline for Anticancer Drug Dosing in Kidney Dysfunction (ADDIKD)**.

| **Renal impairment** |
|---|
| No dose modifications necessary |

| **Hepatic impairment** | |
|---|---|
| **Pre-existing hepatic dysfunction** | |
| Mild | No dose modifications necessary |
| Moderate and Severe | Abiraterone is not recommended |
| **Abiraterone induced hepatotoxicity** | |
| ALT or AST greater than 5 x ULN or bilirubin greater than 3 x ULN | Delay treatment until toxicity has resolved and liver function returns to baseline and restart abiraterone as follows:<br>1st occurrence: Restart abiraterone at 500 mg ONCE daily<br>2nd occurrence: Cease abiraterone |
| ALT 20 x ULN or greater | Cease abiraterone permanently |

| **Hypokalaemia *** | |
|---|---|
| **Serum K+ (mmol/L)** | |
| 3.0 to less than 3.5 | Continue with abiraterone and initiate oral potassium supplementation to maintain K+ |

| Hypokalaemia * | |
|---|---|
| | between 3.5 and 5 mmol/L |
| less than 3.0 | Withhold abiraterone and initiate intravenous potassium and cardiac monitoring |

** Hypokalaemia dose modifications from 'Dosing and Management Guide for Clinicians' for abiraterone, published by the manufacturer.*

| Hypertension | |
|---|---|
| Standard antihypertensive therapy should be commenced and/or adjusted to control blood pressure and/or consider use of the specific mineralocorticoid receptor blocker, eplerenone, to mitigate the toxicity | |
| Grade 3 or Grade 4 | Delay treatment until toxicity has resolved to Grade 1 or less and restart abiraterone as follows:<br>1st occurrence: No dose reduction<br>2nd occurrence: Restart abiraterone at 750 mg ONCE daily<br>3rd occurrence: Restart abiraterone at 500 mg ONCE daily<br>4th occurrence: Cease abiraterone |

## Interactions

*Drug interactions in eviQ protocols are under review and being updated to align with current literature. Further site-wide updates and changes will occur in due course.* ***References & Disclaimer***

*The drug interactions shown below are not an exhaustive list. For a more comprehensive list and for detailed information on specific drug interactions and clinical management, please refer to the specific drug product information and the following key resources:*

- *MIMS - interactions tab (includes link to a CYP-450 table) (login required)*
- *Australian Medicines Handbook (AMH) – interactions tab (login required)*
- *Micromedex Drug Interactions (login required)*
- *Cancer Drug Interactions*
- *Cytochrome P450 Drug Interactions*

| Abiraterone | | |
|---|---|---|
| | **Interaction** | **Clinical management** |
| **Spironolactone** | Reduced efficacy of abiraterone resulting from the ability of spironolactone to bind and activate an androgen receptor, causing abiraterone resistance*<br>*J Clin Oncol 27:3742-3748. 2009 | Avoid combination<br><br>(Note: eplerenone can be used concomitantly with abiraterone) |
| **Potassium lowering drugs (e.g. thiazide diuretics, amphotericin)** | Additive risk of hypokalaemia with abiraterone | Avoid combination or monitor potassium level and for signs of hypokalaemia |
| **Drugs activated by CYP2D6 (e.g. tramadol, codeine, tamoxifen)** | Reduced efficacy of these drugs possible. Abiraterone is a strong inhibitor of CYP2D6 and can reduce transformation of these pro-drugs to active metabolites | Avoid combination |
| **Drugs metabolised by CYP2D6 (e.g. dextromethorphan, beta-blockers, antidepressants, antipsychotics)** | Increased toxicity of these drugs possible due to strong inhibition of CYP2D6 by abiraterone resulting in reduced clearance | Avoid combination or monitor for increased effect/toxicity. Consider dose reduction (esp. of narrow therapeutic index drugs) |
| **CYP3A4 inhibitors (e.g. aprepitant, azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)** | Increased toxicity of abiraterone possible due to reduced clearance | Avoid combination or monitor for abiraterone toxicity |
| **CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)** | Reduced efficacy of abiraterone possible due to increased clearance | Avoid combination or monitor for decreased clinical response to abiraterone |

**Note:**
- Abiraterone is also a strong inhibitor of CYP1A2 and a moderate inhibitor of CYP2C9, CYP2C19 and CYP3A4/5; information about the clinical implications of these interactions is limited and should be considered on a case by case basis
- Abiraterone is an inhibitor of P-glycoprotein (P-gp); plasma concentration of substrates of P-gp may be increased when taken with abiraterone

| Prednisolone | | |
|---|---|---|
| | **Interaction** | **Clinical management** |
| **Antidiabetic agents (e.g. insulin, glibenclamide, glicazide, metformin, pioglitazone, etc)** | The efficacy of antidiabetic agents may be decreased | Use with caution and monitor blood glucose |
| **Azole antifungals (e.g. fluconazole, itraconazole, ketoconazole, posaconazole)** | Increased toxicity of prednisolone possible due to reduced clearance | Avoid combination or monitor for prednisolone toxicity |
| **Oestrogens (e.g. oral contraceptives)** | Increased toxicity of prednisolone possible due to reduced clearance | Avoid combination or monitor for prednisolone toxicity. Dose reduction of prednisolone may be required |
| **Ritonavir** | Increased toxicity of prednisolone possible due to reduced clearance | Avoid combination or monitor for prednisolone toxicity |

| General | | |
|---|---|---|
| | **Interaction** | **Clinical management** |
| **Warfarin** | Anti-cancer drugs may alter the anticoagulant effect of warfarin. | Monitor INR regularly and adjust warfarin dosage as appropriate; consider alternative anticoagulant. |
| **Direct oral anticoagulants (DOACs) e.g. apixaban, rivaroxaban, dabigatran** | Interaction with both CYP3A4 and P-gp inhibitors /inducers.<br><br>DOAC and anti-cancer drug levels may both be altered, possibly leading to loss of efficacy or toxicity (i.e. increased bleeding). | Apixaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors. If treating VTE, avoid use with strong CYP3A4 and P-gp inducers.<br><br>Rivaroxaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors.<br><br>Dabigatran: avoid combination with strong P-gp inducers and inhibitors.<br><br>If concurrent use is unavoidable, monitor closely for efficacy/toxicity of both drugs. |
| **Digoxin** | Anti-cancer drugs can damage the lining of the intestine; affecting the absorption of digoxin. | Monitor digoxin serum levels; adjust digoxin dosage as appropriate. |
| **Antiepileptics** | Both altered antiepileptic and anti-cancer drug levels may occur, possibly leading to loss of efficacy or toxicity. | Where concurrent use of an enzyme-inducing antiepileptic cannot be avoided, monitor antiepileptic serum levels for toxicity, as well as seizure frequency for efficacy; adjust dosage as appropriate. Also monitor closely for efficacy of the anti-cancer therapy. |
| **Antiplatelet agents and NSAIDs** | Increased risk of bleeding due to treatment related thrombocytopenia. | Avoid or minimise combination.<br>If combination deemed essential, (e.g. low dose aspirin for ischaemic heart disease) monitor for signs of bleeding. |
| **Serotonergic drugs, including selective serotonin reuptake inhibitors (SSRIs e.g. paroxetine) and serotonin noradrenaline reuptake inhibitors (SNRIs e.g. venlafaxine)** | Increased risk of serotonin syndrome with concurrent use of 5-HT3 receptor antagonists (e.g. palonosetron, ondansetron, granisetron, tropisetron, dolasetron, etc.) | Avoid combination.<br>If combination is clinically warranted, monitor for signs and symptoms of serotonin syndrome (e.g. confusion, agitation, tachycardia, hyperreflexia).<br>For more information link to TGA Medicines Safety Update |
| **Vaccines** | Diminished response to vaccines and increased risk of infection with live vaccines. | Live vaccines (e.g. BCG, MMR, zoster and varicella) are contraindicated in patients on immunosuppressive therapy. Use with caution in patients on non-immunosuppressive therapy.<br>For more information; refer to the recommended schedule of vaccination for cancer patients, as outlined in the Australian Immunisation Handbook |

## Administration

*eviQ provides safe and effective instructions on how to administer cancer treatments. However, eviQ does not provide every treatment delivery option, and is unable to provide a comprehensive list of cancer treatment agents and their required IV line giving set/filter. There may be alternative methods of treatment administration, and alternative supportive treatments that are also appropriate. Please refer to the individual*

*product information monographs via the TGA website for further information.*

## Administration

**This is a continuous oral treatment**

Safe handling and waste management (reproductive risk only)

Safe administration

General patient assessment prior to each day of treatment.

Any toxicity grade 2 or greater may require dose reduction, delay or omission of treatment and review by medical officer before commencing treatment.

### Treatment - Time out

#### Abiraterone

- administer orally ONCE a day
- to be swallowed whole with a glass of water; do not break, crush or chew
- the administration of abiraterone with food may increase absorption and thus toxicity
- to be taken on an empty stomach, one hour before or two hours after food.

**Note:** missed doses should not be replaced; if a dose is forgotten or vomited, normal dosing should be resumed at the next scheduled dose.

#### Prednisolone

- administer orally TWICE a day (morning and midday) on scheduled days
- to be taken with or after food
- prednisolone can cause sleep disturbance, if this occurs a daily morning dose is recommended.

**Note**: missed doses should not be replaced; if a tablet is forgotten or vomited, normal dosing should be resumed at the next scheduled dose.

**Continue safe handling precautions (reproductive risk only) for 7 days after completion of drug(s).**

## Discharge information

#### Abiraterone tablets

- Abiraterone tablets with written instructions on how to take them.

#### Prednisolone tablets

- Prednisolone tablets with written instructions on how to take them.

#### Patient information

- Ensure patient receives patient information sheet.

# Side effects

*The side effects listed below are not a complete list of all possible side effects for this treatment. Side effects are categorised into the approximate onset of presentation and should only be used as a guide.*

| Immediate (onset hours to days) | |
|---|---|
| **Nausea and vomiting** | Read more about prevention of treatment induced nausea and vomiting |

| Early (onset days to weeks) | |
|---|---|
| **Constipation** | |
| **Diarrhoea** | Read more about treatment induced diarrhoea |
| **Hot flushes** | |
| **Fluid retention and oedema** | An excess amount of fluid around the cells, tissues or serous cavities of the body, leading to swelling. |
| **Hypokalaemia** | Abnormally low levels of potassium in the blood. |
| **Hypertension** | High blood pressure is commonly associated with many anti-cancer drugs. Pre-existing hypertension should be controlled prior to initiation of drugs capable of causing hypertension. |
| **Arthralgia and myalgia** | Generalised joint pain or and/or stiffness and muscle aches, often worse upon waking or after long periods of inactivity. Can improve with movement. May be mild or severe, intermittent or constant and accompanied by inflammation.<br>Read more about arthralgia and myalgia |
| **Fatigue** | Read more about fatigue |
| **Side effects of corticosteroids** | Insomnia, oedema, increased risk of infection e.g. oral thrush, gastric irritation, worsening of peptic ulcer disease, increased blood sugar levels, loss of diabetic control, mood and behavioural changes - including anxiety, euphoria, depression, mood swings, increased appetite and weight gain, osteoporosis and fractures (long term use), bruising and skin fragility are associated with corticosteroid use. |

| Late (onset weeks to months) | |
|---|---|
| **Anaemia** | Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood.<br>Read more about anaemia |

## Evidence

The evidence supporting the use of this protocol comes from two phase III randomised, double-blind, placebo-controlled trials, COU-AA-301[2] (patients who have received prior chemotherapy) and COU-AA-302[3] (chemotherapy naïve patients).

**Post chemotherapy population**

The COU-AA-301 trial was designed to evaluate whether abiraterone plus prednisone compared with placebo plus prednisone prolongs overall survival among patients with metastatic castration-resistant prostate cancer who have received docetaxel. Between May 2008 through July 2009, 1195 patients who had previously received docetaxel were randomly assigned to receive prednisone 5 mg twice daily with either abiraterone acetate 1000 mg or placebo.

The primary end point was overall survival (OS) and the secondary endpoints included time to prostate-specific antigen (PSA) progression and progression-free survival (PFS).[2]

**Chemotherapy naive population**

The COU-AA-302 trial was designed to evaluate whether abiraterone plus prednisolone compared with placebo plus prednisone prolongs radiographic progression free survival and overall survival, among patients with progressive metastatic castrate resistant prostate cancer who had not been previously treated with chemotherapy and with no or mild cancer-related symptoms. Between April 2009 and June 2010, 1088 patients ECOG 0-1, were randomised to receive abiraterone 1000mg (n=546) or placebo (n=542) and prednisolone 5 mg twice daily.

The co-primary endpoints were independently evaluated radiographic progression free survival and overall survival. The secondary end points were patient reported outcomes including, time to opiate use for cancer-related pain, to cytotoxic chemotherapy initiation, to decline in ECOG status and PSA progression.[4]

### Efficacy

#### Post chemotherapy population

Median overall survival was 14.8 months in the abiraterone acetate group and 10.9 months in the placebo group (hazard ratio, 0.65; 95% confidence interval CI, 0.54 to 0.77; P<0.001). Time to PSA progression was 10.2 months in the abiraterone acetate group versus 6.6 months in the placebo group. Median progression free survival on the basis of radiographic evidence was 5.6 months in the abiraterone acetate group versus 3.6 months in the placebo group. Abiraterone acetate significantly increased overall survival compared to placebo.[2]

**Kaplan-Meier curve for overall survival**

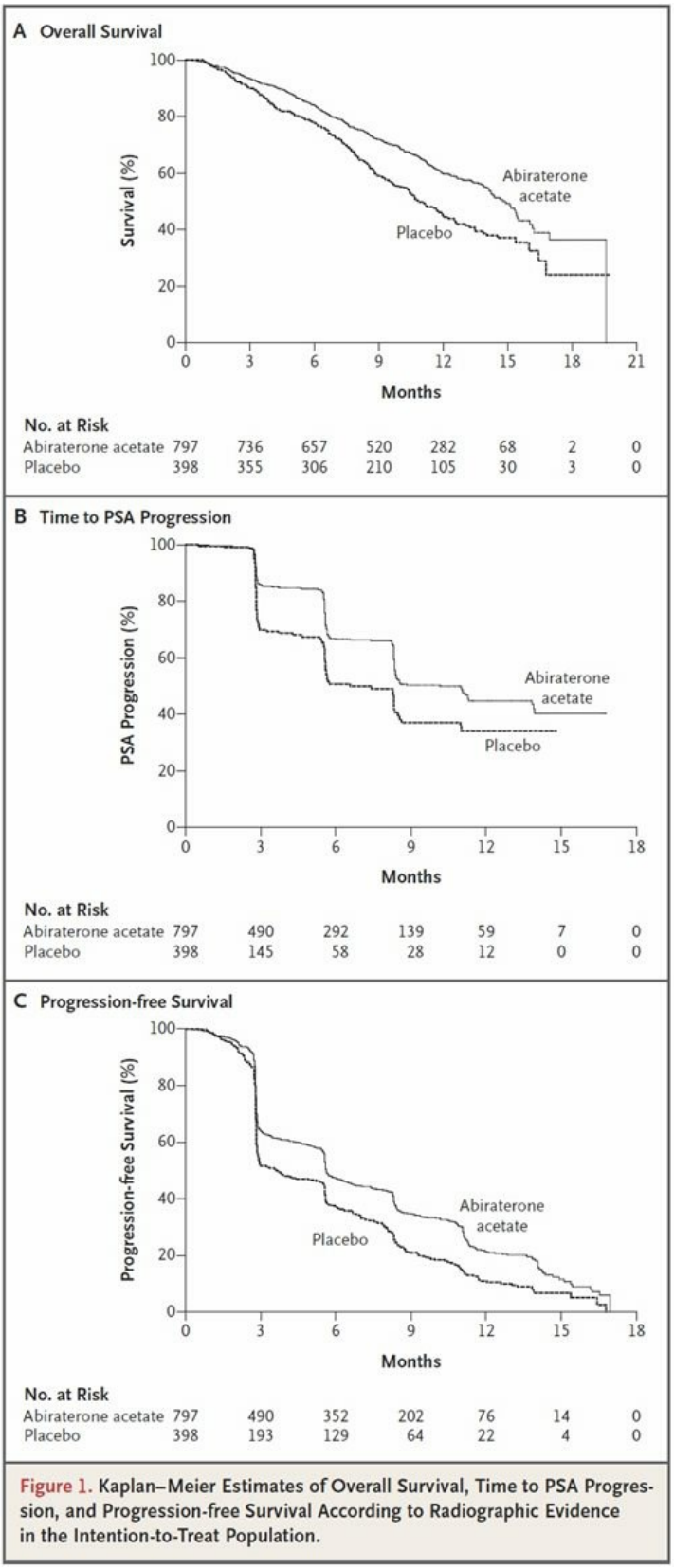



Figure 1. Kaplan–Meier Estimates of Overall Survival, Time to PSA Progression, and Progression-free Survival According to Radiographic Evidence in the Intention-to-Treat Population.



## Chemotherapy naive population

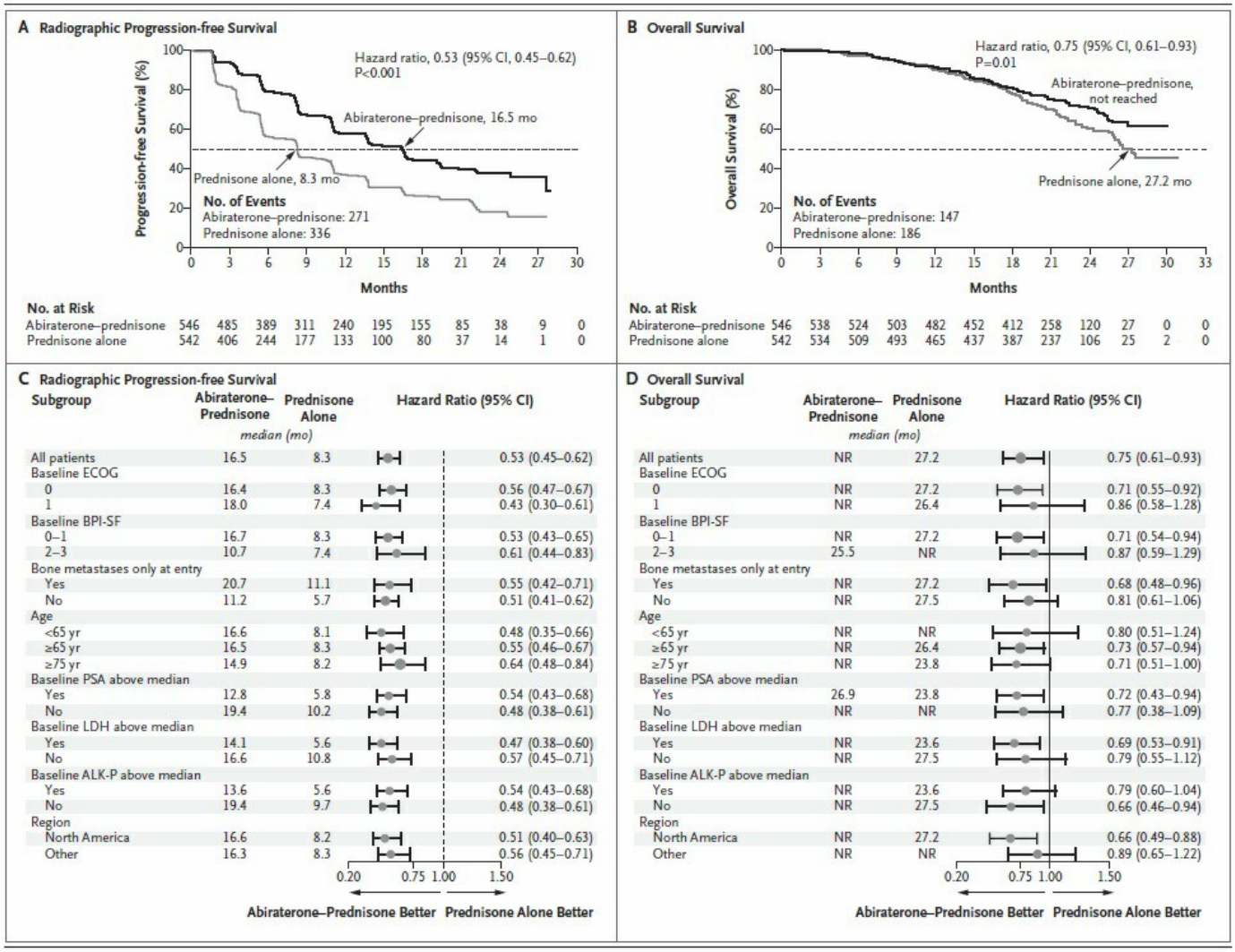
### Radiographic progression[3]

At first interim analysis (when 13% of deaths had occurred) treatment with abiraterone plus prednisolone compared with placebo plus prednisolone, resulted in a 57% reduction in the risk of radiographic progression or death (median not reached v median of 8.3 months; HR for abiraterone/prednisolone -v- prednisolone alone, 0.43; 95% CI 0.35 to 0.52; P<0.001)). By second interim analysis (when 43% of deaths had occurred) the median time to radiographic progression free survival was 16.5 months in the abiraterone plus prednisolone group compared with 8.3 months in the prednisolone only group (HR, 0.53; 95% CI, 0.45 to 0.62; p<0.001).

### Overall Survival[3]

At second interim analysis (22.2 months), more deaths occurred in the prednisolone alone group (186 of 542 patients [34%] -v- 147 of 546 patients [27%]). Median OS was not reached in the abiraterone/prednisolone group -v- 27.2 (95% CI 26.0 to not yet reached) in the prednisolone only group. The risk of death was 25% less in the abiraterone/prednisolone group (HR, 0.75; 95% CI, 0.61 to 0.93; P=0.01).

Final analysis showed a median overall survival of 34.7 months (95% CI 32.7-36.8) in the abiraterone group and 30.3 months (28.7-33.3) in the placebo group. With a significant decrease in risk of death in the abiraterone group compared with the placebo group (HR 0.81, 95% CI 0.70-0.93; p=0.0033).






Secondary endpoints were reported separately.[4]

## Toxicity

The adverse events seen in both trials were minimal and majority occurred at a similar frequency to the control arm – placebo. These adverse events can be attributed to disease or con-current or past therapy such as androgen deprivation therapy (ADT).

Those adverse events seen more frequently in the abiraterone acetate arm included diarrhoea, urinary tract infection, fluid retention and oedema, hypokalemia, hypertension and arthralgia.[2]

**Table 4. Adverse Events.**

| Event | Abiraterone Acetate (N=791) | | | Placebo (N=394) | | |
|---|---|---|---|---|---|---|
| | All Grades | Grade 3 | Grade 4 | All Grades | Grade 3 | Grade 4 |
| | *number (percent)* | | | | | |
| Anemia | 178 (23) | 51 (6) | 8 (1) | 104 (26) | 23 (6) | 6 (2) |
| Thrombocytopenia | 28 (4) | 8 (1) | 3 (<1) | 13 (3) | 1 (<1) | 1 (<1) |
| Neutropenia | 7 (1) | 1 (<1) | 0 | 1 (<1) | 1 (<1) | 0 |
| Febrile neutropenia | 0 | 0 | 0 | 0 | 0 | 0 |
| Diarrhea | 139 (18) | 5 (1) | 0 | 53 (14) | 5 (1) | 0 |
| Fatigue | 346 (44) | 64 (8) | 2 (<1) | 169 (43) | 36 (9) | 3 (1) |
| Asthenia | 104 (13) | 18 (2) | 0 | 52 (13) | 7 (2) | 1 (<1) |
| Back pain | 233 (30) | 44 (6) | 3 (<1) | 129 (33) | 37 (9) | 1 (<1) |
| Nausea | 233 (30) | 12 (2) | 1 (<1) | 124 (32) | 10 (3) | 0 |
| Vomiting | 168 (21) | 13 (2) | 1 (<1) | 97 (25) | 11 (3) | 0 |
| Hematuria | 65 (8) | 11 (1) | 0 | 31 (8) | 9 (2) | 0 |
| Abdominal pain | 95 (12) | 16 (2) | 0 | 44 (11) | 6 (2) | 0 |
| Pain in arm or leg | 134 (17) | 18 (2) | 1 (<1) | 79 (20) | 20 (5) | 0 |
| Dyspnea | 102 (13) | 8 (1) | 2 (<1) | 46 (12) | 7 (2) | 2 (<1) |
| Constipation | 206 (26) | 8 (1) | 0 | 120 (31) | 4 (1) | 0 |
| Pyrexia | 71 (9) | 3 (<1) | 0 | 35 (9) | 5 (1) | 0 |
| Arthralgia | 215 (27) | 33 (4) | 0 | 89 (23) | 16 (4) | 0 |
| Urinary tract infection | 91 (12) | 17 (2) | 0 | 28 (7) | 2 (<1) | 0 |
| Pain | 13 (2) | 5 (1) | 0 | 19 (5) | 6 (2) | 1 (<1) |
| Bone pain | 194 (25) | 42 (5) | 2 (<1) | 110 (28) | 25 (6) | 4 (1) |
| Fluid retention and edema | 241 (31) | 16 (2) | 2 (<1) | 88 (22) | 4 (1) | 0 |
| Hypokalemia | 135 (17) | 27 (3) | 3 (<1) | 33 (8) | 3 (1) | 0 |
| Cardiac disorder* | 106 (13) | 26 (3) | 7 (1) | 42 (11) | 7 (2) | 2 (<1) |
| Liver-function test abnormalities | 82 (10) | 25 (3) | 2 (<1) | 32 (8) | 10 (3) | 2 (<1) |
| Hypertension | 77 (10) | 10 (1) | 0 | 31 (8) | 1 (<1) | 0 |

* Cardiac disorders associated with abiraterone acetate treatment, as defined with the use of the standardized *Medical Dictionary for Regulatory Activities* (version 11.0) queries, included ischemic heart disease, myocardial infarction, supraventricular tachyarrhythmias, ventricular tachyarrhythmias, cardiac failure, and possible arrhythmia-related tests, signs, and symptoms.



**Table 3. Adverse Events of Special Interest.***

| Adverse Event | Abiraterone–Prednisone (N=542) | | Prednisone Alone (N=540) | |
|---|---|---|---|---|
| | Grade 1–4 | Grade 3 or 4 | Grade 1–4 | Grade 3 or 4 |
| Fluid retention or edema | 150 (28) | 4 (<1) | 127 (24) | 9 (2) |
| Hypokalemia | 91 (17) | 13 (2) | 68 (13) | 10 (2) |
| Hypertension | 118 (22) | 21 (4) | 71 (13) | 16 (3) |
| Cardiac disorder† | 102 (19) | 31 (6) | 84 (16) | 18 (3) |
| Atrial fibrillation | 22 (4) | 7 (1) | 26 (5) | 5 (<1) |
| ALT increased | 63 (12) | 29 (5) | 27 (5) | 4 (<1) |
| AST increased | 58 (11) | 16 (3) | 26 (5) | 5 (<1) |

* Adverse events of special interest were selected on the basis of the safety profile of phase 2 and phase 3 studies of abiraterone. ALT denotes alanine aminotransferase, and AST aspartate aminotransferase.
† Cardiac disorders included ischemic heart disease, myocardial infarction, supraventricular tachyarrhythmia, ventricular tachyarrhythmia, cardiac failure, and possible arrhythmia-related investigations, signs, and symptoms.

## References


1 Aapro, M. and F. Saad. 2012. "Bone-modifying agents in the treatment of bone metastases in patients with advanced genitourinary malignancies: a focus on zoledronic acid." Ther Adv Urol 4(2):85-101.

2 de Bono, J. S., C. J. Logothetis, A. Molina, et al. 2011. "Abiraterone and increased survival in metastatic prostate cancer." N Engl J Med 364(21):1995-2005.

3 Ryan, C. J., M. R. Smith, J. S. de Bono, et al. 2013. "Abiraterone in metastatic prostate cancer without previous chemotherapy." N Engl J Med 368(2):138-148.

4 Basch, E., K. Autio, C. J. Ryan, et al. 2013. "Abiraterone acetate plus prednisone versus prednisone alone in chemotherapy-naive men with metastatic castration-resistant prostate cancer: patient-reported outcome results of a randomised phase 3 trial." Lancet Oncol 14(12):1193-1199.


### Bibliography


Attard, G., A. H. Reid, R. A'Hern, et al. 2009. "Selective inhibition of CYP17 with abiraterone acetate is highly active in the treatment of castration-resistant prostate cancer." J Clin Oncol 27(23):3742-3748.


## History

### Version 4

| Date | Summary of changes |
|---|---|
| **10/09/2020** | Patient information title updated- 'hormone resistant' added. Version number changed to V.4. |
| **21/12/2021** | Changed antiemetic clinical information block to minimal or low, to align with new categories. See ID 7 Prevention of anti-cancer therapy induced nausea and vomiting (AINV) v5. |

### Version 3

| Date | Summary of changes |
|---|---|
| **30/11/2012** | New protocol taken to Medical Oncology Reference Committee meeting. |
| **09/05/2013** | Approved and published on eviQ. |
| **09/05/2014** | Reviewed by Medical Oncology Reference Committee electronically. No changes. PHC view removed. Review 2 years. |
| **16/12/2014** | Indications updated in line with TGA broadened indications. |
| **23/07/2015** | Patient sheet updated. |
| **31/05/2017** | Transferred to new eviQ website. Protocol version number changed to V.2. |
| **30/8/2017** | Protocol reviewed by Reference Committee:<br>• Prednisolone dose changed to 10 mg daily with a note that 5 mg twice daily can be given.<br>• Dexamethasone note added as another steroid option.<br>• Patient information reviewed and side effect section changed to a table showing limited difference between the drug and placebo.<br>• Evidence section updated |
| **30/11/2017** | Link to Androgen Deprivation Therapy (ADT) patient information sheet added to protocol and patient information. |
| **10/10/2018** | Treatment schedule note and drug status updated to include 500 mg tablets. |
| **02/04/2019** | Protocol reviewed at Medical Oncology Reference Committee meeting on 15/03/2019. Title updated to include castration resistant. Indications updated to include ECOG. ID 3580 Prostate metastatic castration sensitive abiraterone and prednisolone added as a related page. Patient information updated -your treatment and when to get help changed to less chemotherapy focused information. Protocol version number changed to V.3. Next review in 5 years. |

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# Patient information - Prostate cancer metastatic hormone-resistant - Abiraterone and prednisolone

**Patient's name:**

## Your treatment

It is important to understand that abiraterone is not a traditional chemotherapy drug and has a different way of working. It works by targeting the cancer cells to stop them growing and spreading. The treatment schedule below explains how the drug for this treatment is given.

| **Abiraterone and prednisolone** | | |
|---|---|---|
| This treatment is continuous. Your doctor will advise you how long to take the treatment for. | | |
| **Day** | **Treatment** | **How it is given** |
| Continuous | **Abiraterone** (*a-bir-A-ter-one)* | Take orally (dose 1000 mg, see table below) ONCE a day on an empty stomach, one hour before food or 2 hours after food. Swallow whole with a glass of water, do not break, crush or chew. |
| | **Prednisolone** (*pred-NIS-oh-lone*) | Take orally with or after food. |

Abiraterone tablets are available in two tablet strengths, 250 mg and 500 mg. It is important that you take the correct tablets and understand how to take them. Ask your doctor, nurse or pharmacist to complete the table below with the correct number of tablets for you.

| Abiraterone | Number of tablets |
|---|---|
| 250 mg tablets | |
| 500 mg tablets | |

**Missed doses:**

- **Abiraterone** or **prednisolone** : if you forget to take a tablet or vomit a tablet, take your normal dose the next time it is due. Do not take an extra dose.

## When to get help

Anticancer drugs (drugs used to treat cancer) can sometimes cause serious problems. It is important to get medical help immediately if you suddenly become unwell.

**Emergency contact details**

Ask your doctor or nurse from your treating team when you should get help and who to contact if you have a problem

Daytime: .....

Night/weekend: .....

Other instructions: .....

.....

.....

## Other information about your treatment

### Changes to your dose or treatment delays

Sometimes a treatment may be started at a lower dose or the dose needs to be changed during treatment. There may also be times when your treatment is delayed. This can happen if your doctor thinks you are likely to have severe side effects, if you get severe side effects, if your blood counts are affected and causing delays in treatment, or if you are finding it hard to cope with the treatment. This is called a dose reduction, dose change or treatment delay. Your doctor will explain if you need any changes or delays to your treatment and the reason why.

### Blood tests and monitoring

You may need to have blood tests while you are receiving this treatment. Your doctor or nurse will tell you when to have these blood tests.

### Androgen deprivation therapy (ADT)

For more information see the eviQ patient information sheet on Androgen deprivation therapy (ADT) for prostate cancer.

## Side effects

This treatment has minimal side effects. In the clinical trial when abiraterone was compared with a dummy tablet (placebo) very few side effects were caused by abiraterone. Most of the symptoms that patients had were due to their prostate cancer. Below is a table of possible side effects you may get with this treatment. Remember most of these side effects are temporary and can be managed. Some people have more side effects than others, everyone is different. If you are worried about any of your symptoms, contact your doctor or nurse

| Symptoms | Abiraterone - Moderate or severe (%) | Placebo - Moderate or severe (%) |
|---|---|---|
| **Heart problems** | 3-6 | 2-3 |
| **Low blood potassium levels*** | 2-3 | 1-2 |
| **High liver blood tests** | 3-8 | <1-3 |
| **Fluid retention and swelling** | 1-2 | 1 |
| **Urinary tract infection** | 2 | <1 |
| **High blood pressure (hypertension)** | 1-5 | <1-3 |
| **Bleeding and bruising (thrombocytopenia)** | 1 | <1 |

* Low blood potassium levels may be found from your routine blood tests and treated by your doctor. If it is severe you may get muscle cramps or twitches, constipation, confusion or an irregular heartbeat. Tell your doctor or nurse as soon as possible if you get any of these signs or symptoms.

## General advice for people having cancer treatment

### Blood clot risk

- Cancer and anticancer drugs can increase the risk of a blood clot (thrombosis).
- Tell your doctor if you have a family history of blood clots.
- A blood clot can cause pain, redness, swelling in your arms or legs, shortness of breath or chest pain.
- If you have any of these symptoms go to your nearest hospital Emergency Department.

### Medications and vaccinations

- Before you start treatment, tell your doctor about any medications you are taking, including vitamins or herbal supplements.

- Don't stop or start any medications during treatment without talking to your doctor and pharmacist first.
- Vaccinations such as flu and tetanus vaccines are safe to receive while you are having treatment. If you are unsure, check with your doctor before you have any vaccinations.

### Other medical and dental treatment

- If you go to hospital or any other medical appointment (including dental appointments), always tell the person treating you that you are receiving anticancer drugs.
- Before you have any dental treatment, talk to your doctor.

### Diet

- While you are receiving this treatment it is important that you try to maintain a healthy diet.
- Grapefruit and grapefruit juice can interact with your medication and should be avoided while you are on this treatment.
- Speak to your doctor or nurse about whether drinking alcohol is safe with your treatment.
- If you have any concerns about recent weight loss or weight gain or questions about your diet, ask to speak to a dietitian.

### Fertility

- Some cancer treatments can reduce your fertility. This can make it difficult or impossible to father a child.
- Talk to your doctor or nurse before you start any treatment. Depending on your situation there may be fertility sparing options available to you and/or your partner, discuss these with your doctor or nurse.

### Fathering a child

- Some cancer treatments can be dangerous to unborn babies. Talk to your doctor or nurse if you think there is any chance that your partner could be pregnant.
- Do not try to father a child during this treatment. Contraception should be used during treatment and after stopping treatment. Ask your doctor or nurse about what type of contraception you should use.
- If you are planning fatherhood after completing this treatment, talk to your doctor. Some doctors advise waiting between 6 months and 2 years after treatment.

### Sex life and sexuality

- The desire to have sex may decrease as a result of this treatment or its side effects.
- Your emotions and the way you feel about yourself may also be affected by this treatment.
- It may help to discuss your concerns with your partner and doctor or nurse.

### Quitting smoking

- It is never too late to quit smoking. Quitting smoking is one of the best things you can do to help your treatment work better.
- There are many effective tools to improve your chances of quitting.
- Talk to your treating team for more information and referral to a smoking cessation support service.

### Staying active

- Research shows that exercise, no matter how small, has many benefits for people during and after cancer treatment.
- Talk to your doctor before starting an exercise program. Your doctor can advise whether you need a modified exercise program.

**For more information about cancer treatment, side effects and side effect management see our Patient and carers section.**

## Where to get more information

### Telephone support

- Call Cancer Council on 13 11 20 for cancer information and support

### Prostate cancer information

- Continence Foundation of Australia – continence.org.au
- Healthy Male Andrology Australia – healthymale.org.au
- National Continence Management Strategy – bladderbowel.gov.au/ncp/ncms
- National Public Toilet Map – toiletmap.gov.au
- Prostate Cancer Foundation of Australia – prostate.org.au
- South Australian Prostate Cancer Clinical Outcome Collaborative – prostatehealth.org.au

### General cancer information and support

- Australian Rare Cancer (ARC) Portal – arcportal.org.au/
- Beyondblue – beyondblue.org.au
- Cancer Australia – canceraustralia.gov.au
- Cancer Council Australia – cancer.org.au
- Cancer Voices Australia – cancervoicesaustralia.org
- CanTeen – canteen.org.au
- Carers Australia – carersaustralia.com.au
- CHILL Cancer related hair loss - scalpcooling.org
- eviQ Cancer Treatments Online – eviQ.org.au
- LGBTQI+ People and Cancer - cancercouncil.com.au/cancer-information/lgbtqi
- Look Good Feel Better – lgfb.org.au
- Patient Information – patients.cancer.nsw.gov.au
- Radiation Oncology Targeting Cancer – targetingcancer.com.au
- Redkite – redkite.org.au
- Return Unwanted Medicines – returnmed.com.au
- Staying active during cancer treatment – patients.cancer.nsw.gov.au/coping-with-cancer/physical-wellbeing/staying-active

### Quit smoking information and support

Quitting smoking is helpful even after you have been diagnosed with cancer. The following resources provide useful information and support to help you quit smoking. Talk to your treating team about any other questions you may have.

- Call Quitline on 13 QUIT (13 78 48)
- iCanQuit – iCanQuit.com.au
- Patient Information – patients.cancer.nsw.gov.au/coping-with-cancer/physical-wellbeing/quitting-smoking
- Quitnow – quitnow.gov.au

**Additional notes:**

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