

# Non small cell lung cancer locally advanced or metastatic atezolizumab

ID: 3408 v.4 Endorsed

Treatment must be initiated and supervised by specialist physicians experienced in the treatment of cancer using immunological agents. Before commencing immunotherapy treatment in any patient, clinicians should have an understanding of the immune-related adverse events (irAEs) associated with immunotherapy treatment and their management.

Check for clinical trials in this patient group. Link to [Australian Clinical Trials](#) website

Link to [Clinical practice guidelines for the treatment of lung cancer](#)

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](#).

## International Consensus Guideline for Anticancer Drug Dosing in Kidney Dysfunction (ADDIKD)

2022

[Click here](#)



### Treatment schedule - Overview

#### Cycle 1 and further cycles

Drug	Dose	Route	Day
Atezolizumab	1,200 mg *	IV infusion	1

\* Alternative dosing schedule 1680 mg every 28 days<sup>1</sup>

**Frequency:** 21 days

**Cycles:** Continuous until disease progression or unacceptable toxicity

#### Notes:

In the first few months after the start of immunotherapy, some patients can experience transient tumour flare (termed "pseudo progression" or an immune response). This may manifest as growth of existing lesions or the development of new lesions prior to later tumour regression. While this is rare (~5%), continuing treatment and performing a second scan 4 to 6 weeks later to confirm progression may be considered, particularly if the patient remains well.

Radiation recall has been observed with PD-L1 inhibitors, consideration should be given to the timing when starting this treatment after a prolonged course of radiation therapy.

**Drug status:** Atezolizumab is [PBS authority](#)

Atezolizumab is TGA registered but not PBS listed for patients who have received prior treatment with a programmed cell death-1 (PD-1) inhibitor or a programmed cell death ligand-1 (PD-L1) inhibitor for this condition

**Cost:** ~ \$6,840 per cycle

### 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.](#)

## Cycle 1 and further cycles

Day 1		
Atezolizumab	1,200 mg (IV infusion)	in 250 mL sodium chloride 0.9% over 60 minutes ; if first dose is well tolerated, subsequent doses may be administered over 30 minutes

**Note:** Alternative dosing schedule 1680 mg every 28 days<sup>1</sup>

**Frequency:** 21 days

**Cycles:** Continuous until disease progression or unacceptable toxicity

## Indications and patient population

### Indications:

- Palliative treatment of locally advanced or metastatic non small cell lung cancer (NSCLC) with progression on or after prior platinum chemotherapy.
- In patients with non-squamous NSCLC epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genomic aberrations, patients should have also received both targeted therapy and platinum chemotherapy.
- ECOG performance status score 0 or 1.

### Precautions:

If any of these conditions are present, clinical judgement should be used and individual cases discussed with an expert in the field as indicated:

- significant autoimmune disease (e.g. myasthenia gravis, inflammatory bowel disease, systemic lupus erythematosus, rheumatoid arthritis, autoimmune ocular disease)
- organ transplantation
- previous history of viral hepatitis
- HIV/acquired immune deficiency syndrome (AIDS)
- previous radiation to the lungs.

## Clinical information

<b>Venous access required</b>	IV cannula (IVC) or central venous access device (CVAD) is required to administer this treatment. Read more about <a href="#">central venous access device line selection</a>
<b>Emetogenicity MINIMAL</b>	No antiemetics should be routinely administered before treatment in patients without a history of nausea and vomiting. If patients experience nausea and/or vomiting, consider using the low antiemetic prophylaxis regimen. Read more about <a href="#">preventing anti-cancer therapy induced nausea and vomiting</a>

<b>Immune-related adverse events (irAEs)</b>	<p>Immune-related adverse events (irAEs) can occur early and escalate quickly in patients receiving immune checkpoint inhibitors. irAEs can also occur after discontinuation of treatment. Fatalities have been reported. Management of irAEs is largely based on expert opinion and consensus guidelines.</p> <p>Examples of irAEs with high risk of mortality include:</p> <ul style="list-style-type: none"> <li>• cardiac toxicity: myocarditis</li> <li>• musculoskeletal toxicity: myositis</li> <li>• neurological toxicity: encephalitis, Guillain-Barré syndrome, myelitis, myasthenia gravis</li> <li>• pulmonary toxicity: pneumonitis</li> <li>• skin toxicity: Steven-Johnson syndrome, toxic epidermal necrolysis.</li> </ul> <p>Examples of irAEs in order of frequency include:</p> <ul style="list-style-type: none"> <li>• Common <ul style="list-style-type: none"> <li>◦ endocrinopathies: thyroid dysfunction</li> <li>◦ gastrointestinal toxicity: diarrhoea</li> <li>◦ musculoskeletal toxicity: arthralgia, myalgia</li> <li>◦ skin toxicity: rash, erythema, pruritus</li> </ul> </li> <li>• Less common <ul style="list-style-type: none"> <li>◦ endocrinopathies: hypophysitis, type I diabetes mellitus</li> <li>◦ gastrointestinal toxicity: colitis</li> <li>◦ musculoskeletal toxicity: inflammatory arthritis</li> <li>◦ ocular toxicity: dry eye</li> <li>◦ renal toxicity</li> <li>◦ skin toxicity: vitiligo</li> </ul> </li> <li>• Rare <ul style="list-style-type: none"> <li>◦ endocrinopathies: primary adrenal insufficiency</li> <li>◦ gastrointestinal toxicity: pancreatitis</li> <li>◦ haematological toxicity</li> <li>◦ musculoskeletal toxicity: vasculitis</li> <li>◦ ocular toxicity: uveitis, iritis.</li> </ul> </li> </ul> <p>Proactive monitoring, patient self-monitoring and early reporting of adverse events is critical. Treatment interruptions/discontinuation, consultation with specialist and administration of corticosteroids and/or supportive care is required to minimise the risk of death.</p> <p>Read more about the <a href="#">management of immune-related adverse events (irAEs)</a></p>
<b>Baseline investigations</b>	<p>Consider ECG and troponin at baseline. There is no clear evidence regarding the efficacy/value of baseline ECG or troponin in patients receiving immune checkpoint inhibitor therapy. Some cancer specialists obtain baseline testing, and others continue this through the initial period of therapy. Consider urinalysis at baseline, particularly in patients with additional risk factors for developing immune-related acute kidney injury.</p>
<b>Blood tests</b>	<p>FBC, EUC, eGFR, LFTs, serum cortisol, TFTs and BSL at baseline.</p> <p>Repeat FBC, EUC, eGFR, LFTs and BSL prior to each cycle and serum cortisol and TFTs alternate cycles. Check lipase and amylase if symptomatic of pancreatitis.</p> <p>In the absence of suspicion of immune-related adverse events less frequent monitoring may be applicable, according to institutional guidelines. Evidence for the frequency of routine blood testing with immunotherapies varies within published studies and guidelines.</p> <p>Read more about <a href="#">immunotherapy blood test monitoring recommendations</a>.</p>
<b>Hepatitis and HIV</b>	<p>Hepatitis screening is recommended in all patients who are to receive immune checkpoint inhibitors.</p> <p>Immunotherapy is associated with inflammatory adverse reactions resulting from increased or excessive immune activity and patients are at risk of developing autoimmune hepatitis. It should be used with caution in patients who have a history of chronic hepatic infections (hepatitis B and C), detectable human immunodeficiency virus (HIV) viral load or acquired immune deficiency syndrome (AIDS).</p>

<b>Vaccinations</b>	The safety of having vaccinations during treatment is unknown. Patients in the clinical trials were typically allowed to receive inactivated and recombinant vaccines but not live vaccines. Read more about <a href="#">COVID-19 vaccines and cancer</a> .
<b>Effects of cancer treatment on fertility</b>	Studies to evaluate the effects of immune checkpoint inhibitor therapy on fertility have not been performed. Therefore, the effect on male and female fertility is unknown. Limited evidence supports that immune checkpoint inhibitor-related hypogonadism due to orchitis and hypophysitis can impact fertility. Immune checkpoint inhibitors can cause fetal harm when given to pregnant women. A pregnancy test should be considered in females of reproductive potential if sexually active. It is important that all patients of reproductive potential use effective contraception whilst on therapy and after treatment finishes. There is very limited evidence to provide guidance regarding contraception timelines. Some studies have demonstrated PD-1 receptor occupancy for greater than 9 months after anti-PD-1 therapy (Brahmer et al., 2010). As a result, some cancer specialists advise using contraception for at least six months or even as long as two years after treatment finishes. Read more about the <a href="#">effect of cancer treatment on fertility</a> Link to <a href="#">Brahmer et al., 2010</a>

## 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.*

- Dose reduction is not recommended
- No dose adjustment is required in the elderly, mild or moderate renal impairment or mild hepatic impairment. Immune checkpoint inhibitors have not been studied in patients with severe renal impairment or moderate to severe hepatic impairment.

### Management of immune-related adverse events (irAEs)

Link to [Management of immune-related adverse events \(irAEs\)](#)

## 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](#)

### Atezolizumab

**No formal pharmacokinetic drug interaction studies have been conducted with atezolizumab.**

	<b>Interaction</b>	<b>Clinical management</b>
<b>Immunosuppressants (inc.</b>	Reduced efficacy of both	It is recommended that patients

Atezolizumab		
corticosteroids)	immunosuppressants and atezolizumab possible due to pharmacodynamic interaction	<p>requiring corticosteroids <b>prior</b> to treatment receive the lowest possible dose (preferably no greater than 10 mg prednisolone or equivalent steroid per day). <b>Once started</b> on atezolizumab the use of corticosteroids to treat immune related adverse events (irAEs) does not appear to impact the clinical response to atezolizumab. In patients requiring ongoing corticosteroids <b>post management</b> of an irAE, the dose should be as low as possible.</p> <p>Monitor for signs of organ rejection in transplant recipients.</p>

## 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.*

### Day 1

**Approximate treatment time: 90 minutes (initial); 60 minutes (subsequent)**

[Handling of monoclonal antibodies and waste management](#)

[Safe administration](#)

[Immunotherapy patient assessment](#) prior to each treatment.

Any toxicity may require delay of treatment and review by medical officer before commencing treatment.

Prime IV line(s).

Insert IV cannula or access [TIVAD](#) or [CVAD](#).

#### Pre treatment medication

Administer antiemetics if required

#### Treatment - Time out

#### Atezolizumab

- atezolizumab has a short expiry- 8 hours at room temperature and 24 hours when refrigerated

#### Administer atezolizumab:

- via IV infusion over 60 minutes for first infusion. If the first infusion is tolerated, all subsequent infusions may be administered over 30 minutes
- flush with 50 mL of sodium chloride 0.9%

#### Mild or moderate (grade 1 or 2) infusion-related reaction:

- decrease the rate of infusion and monitor closely
- give any further doses with close monitoring
- premedication with paracetamol and an antihistamine should be considered for further doses

#### Severe (grade 3 or 4) infusion-related reaction:

- stop infusion immediately
- medical officer review
- permanently discontinue atezolizumab

Remove IV cannula and/or deaccess [TIVAD](#) or [CVAD](#).

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## Discharge information

### 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.*

The most common side effects with this treatment are immune-related adverse events (irAEs). irAEs can escalate quickly and close monitoring of the patient is required. Symptoms should improve promptly after the introduction of immunosuppressive therapy. If this does not occur review the diagnosis and seek further specialist advice. Refer to the [Management of immune related adverse events](#) document for further information.

Immune related adverse events	
<b>Cardiotoxicity</b>	<p>Cardiotoxicity is a rare but serious side effect, which may manifest as asymptomatic reduction in left ventricular ejection fraction (LVEF), arrhythmia, cardiomyopathy, myocarditis, pericarditis, cardiac fibrosis, hypertension, cardiac ischaemia, congestive heart failure (CHF) and cardiac arrest.</p> <p>Read more about <a href="#">Management of immune related adverse events</a>.</p>
<b>Gastrointestinal toxicity</b>	<p>Colitis, diarrhoea or more bowel movements than usual; blood or mucous in stools; dark, tarry, sticky stools; abdominal pain or tenderness.</p> <p>Read more about <a href="#">Management of immune related adverse events</a></p>
<b>Haematological toxicity</b>	<p>Autoimmune haemolytic anaemia (AIHA), acquired thrombotic thrombocytopenic purpura (TTP), aplastic anaemia (AA), immune thrombocytopenia (ITP), acquired haemophilia (AH), haemolytic uremic syndrome (HUS) and lymphopenia are rare but potentially serious immune-related adverse events associated with immunotherapy treatment.</p> <p>Read more about <a href="#">Management of immune related adverse events</a>.</p>
<b>Hepatotoxicity</b>	<p>Transaminase and total bilirubin elevation, jaundice, severe nausea or vomiting, pain on the right side of the abdomen, drowsiness, dark urine, bleeding or bruising more easily than normal, anorexia.</p> <p>Read more about <a href="#">Management of immune related adverse events</a>.</p>
<b>Musculoskeletal toxicity</b>	<p>Inflammatory arthritis, temporal arteritis, arthralgia, myalgia, synovitis, vasculitis, polymyalgia-like syndrome and myositis.</p> <p>Read more about <a href="#">Management of immune related adverse events</a>.</p>
<b>Neurological toxicity</b>	<p>Aseptic meningitis, myasthenia gravis, Guillain-Barre syndrome, encephalitis, meningeal symptoms, optic neuritis, neuropathy and acute inflammatory demyelinating polyneuropathy are infrequent but potentially serious immune-related adverse events associated with immunotherapy treatment.</p> <p>Read more about <a href="#">Management of immune related adverse events</a>.</p>
<b>Ocular toxicity</b>	<p>Eye pain, blurred vision, Uveitis/iritis, episcleritis, blepharitis, optic neuritis, tear duct stenosis, conjunctivitis, hyperlacrimation, watery or dry eyes and photophobia.</p> <p>Read more about <a href="#">Management of immune related adverse events</a>.</p>
<b>Other endocrinopathies</b>	<p>Type 1 diabetes mellitus, hypophysitis, hypopituitarism and adrenal insufficiency are infrequent but potentially serious immune-related adverse events associated with immunotherapy treatment.</p> <p>Read more about <a href="#">Management of immune related adverse events</a></p>
<b>Pulmonary toxicity</b>	<p>Radiographic changes, dyspnoea, new or worsening cough, hypoxia, tachycardia, chest pain or fever.</p> <p>Read more about <a href="#">Management of immune related adverse events</a>.</p>
<b>Renal toxicity</b>	<p>Increase in serum creatinine, oliguria, haematuria, peripheral oedema and anorexia.</p> <p>Read more about <a href="#">Management of immune related adverse events</a>.</p>
<b>Skin toxicity</b>	<p>Rash including full thickness, pruritus, skin blisters, ulceration and necrosis. Radiation recall can occur at site of previous radiation therapy. Symptoms include vesiculation, desquamation and ulceration of the skin.</p> <p>Read more about <a href="#">Management of immune related adverse events</a></p>
<b>Thyroid toxicity</b>	<p>Thyroid toxicity is common with immune checkpoint inhibitors. Hypothyroidism is most frequent however hyperthyroidism can also occur.</p> <p>Read more about <a href="#">Management of immune related adverse events</a></p>

Non-immune related adverse events	
<b>Nausea and vomiting</b>	Read more about <a href="#">prevention of treatment induced nausea and vomiting</a>
<b>Fatigue</b>	Read more about <a href="#">fatigue</a>
<b>Fever</b>	
<b>Flu-like symptoms</b>	
<b>Anorexia</b>	Loss of appetite accompanied by decreased food intake. Read more about <a href="#">anorexia</a>

## Evidence

The evidence supporting this protocol is provided by a phase 3 multicentre international randomised trial (OAK) involving 1225 patients comparing atezolizumab with docetaxel alone in patients with Stage IIIB and IV non-small cell lung cancer who had progressed on or after one platinum-containing chemotherapy regime.<sup>2</sup>

Between March 2014 and April 2015, 613 patients were randomised to receive atezolizumab 1200 mg every three weeks and 612 patients were randomised to receive docetaxel 75 mg/m<sup>2</sup> every three weeks until unacceptable toxicity or disease progression.

The primary end point was overall survival (OS) and secondary end points were investigator-assessed progression-free survival (PFS), proportion of patients who had an objective response (ORR), duration of response, and safety.

### Efficacy

After a median follow up of 21 months, the median OS was 13.8 months in the atezolizumab arm versus 9.6 months in the docetaxel arm (HR= 0.73; 95% CI: 0.62 to 0.87; p= 0.0003). 425 patients in each the atezolizumab and docetaxel groups were included in the primary efficacy analysis (first 850 patients).

**Table 1: Summary of key efficacy results<sup>2</sup>**

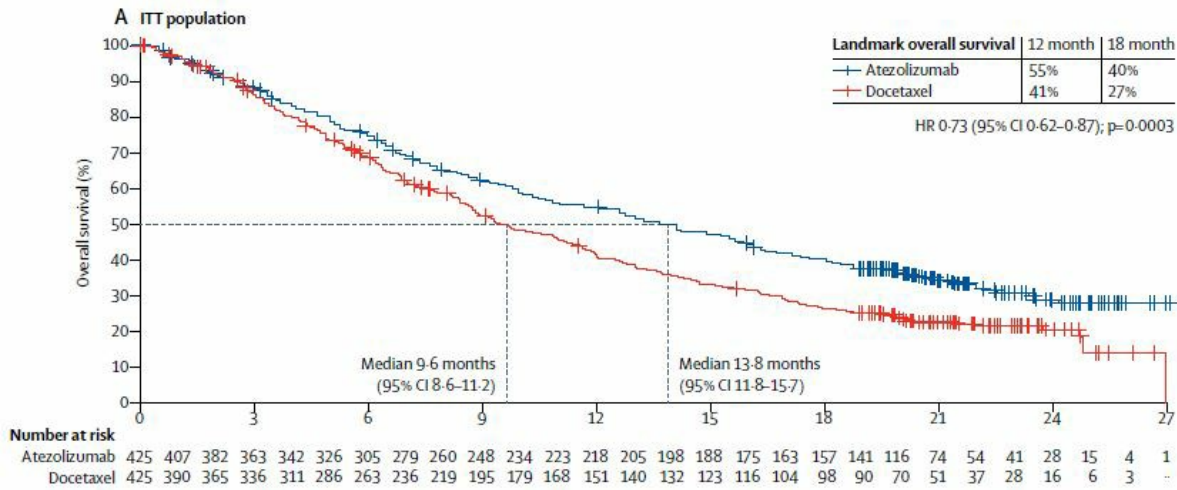
	Atezolizumab (n=425)	Docetaxel (n=425)	HR (95% CI)	p value
<b>Progression-free survival (ITT population)</b>				
Patients with event (%)	380 (89%)	375 (88%)	0.95 (0.82–1.10)	0.49
Median (months; 95% CI)	2.8 (2.6–3.0)	4.0 (3.3–4.2)	..	..
<b>Objective response rate (ITT population)</b>				
Objective response (%)	58 (14%)	57 (13%)	..	..
Complete response (%)	6 (1%)	1 (<1%)	..	..
Partial response (%)	52 (12%)	56 (13%)	..	..
Stable disease (%)	150 (35%)	177 (42%)	..	..
Progressive disease (%)	187 (44%)	117 (28%)	..	..
Missing or unevaluable (%)	30 (7%)	74 (17%)	..	..
<b>Duration of response (ITT population)*</b>				
Median (months; 95% CI)	16.3 (10.0–NE)	6.2 (4.9–7.6)	0.34 (0.21–0.55)	<0.0001
<b>Progression-free survival (TC1/2/3 or IC1/2/3)</b>				
Patients with event (%)	216/241 (90%)	193/222 (87%)	0.91 (0.74–1.12)	0.38
Median (months; 95% CI)	2.8 (2.6–4.0)	4.1 (2.9–4.3)	..	..
<b>Objective response (TC1/2/3 or IC1/2/3)</b>				
Objective response	43/241 (18%)	36/222 (16%)	..	..
Complete response	5/241 (2%)	1/222 (<1%)	..	..
Partial response	38/241 (16%)	35/222 (16%)	..	..
Stable disease	79/241 (33%)	85/222 (38%)	..	..
Progressive disease	102/241 (42%)	59/222 (27%)	..	..
Missing or unevaluable	17/241 (7%)	42/222 (19%)	..	..
<b>Duration of response (TC1/2/3 or IC1/2/3)†</b>				
Median (months; 95% CI)	16.0 (9.7–NE)	6.2 (4.9–9.2)	0.38 (0.22–0.65)	0.0003

HR was stratified for progression-free survival in the ITT and TC1/2/3 or IC1/2/3 populations; unstratified for other subgroups and duration of response. \* n=58 for the atezolizumab group and n=57 for the docetaxel group. † n=43 for the atezolizumab group and n=36 for the docetaxel group. HR=hazard ratio. IC=tumour infiltrating immune cells. ITT=intention-to-treat. NE=not evaluable. TC=tumour cell.

**Table 2: Summary of key efficacy results**



Figure 1: Kaplan- Meier for overall survival in the intention-to-treat population<sup>2</sup>



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## Toxicity

Treatment was discontinued for adverse reactions in 8% of atezolizumab patients and 19% of docetaxel patients. 25% of patients receiving atezolizumab had a drug delay for an adverse reaction. Treatment related grade 3 or 4 adverse events occurred in 15% of patients receiving atezolizumab and in 43% of patients receiving docetaxel. There were no atezolizumab related deaths and one docetaxel related death reported.

Table 2: Summary of adverse events<sup>2</sup>

	Atezolizumab (n=609)	Docetaxel (n=578)
All adverse events	573 (94%)	555 (96%)
Treatment-related adverse events	390 (64%)	496 (86%)
Grade 3 or 4 adverse events	227 (37%)	310 (54%)
Treatment-related grade 3 or 4 adverse events	90 (15%)	247 (43%)
All deaths	10 (2%)	14 (2%)
Treatment-related death	0	1 (<1%)*
Serious adverse events	194 (32%)	181 (31%)
Adverse events leading to withdrawal from treatment	46 (8%)	108 (19%)
Adverse events leading to dose modification, delay, or interruption	152 (25%)	210 (36%)

\*One death due to a respiratory tract infection.

Table 3: Summary of adverse events in the safety population

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Table 3: Adverse events reported<sup>3</sup>

Adverse event	Atezolizumab n=609		Docetaxel n=578	
	Any grade	Grade 3 or 4	Any grade	Grade 3 or 4
Fatigue	163 (26·8)	17 (2·8)	205 (35·5)	23 (4·0)
Decreased appetite	143 (23·5)	2 (0·3)	136 (23·5)	9 (1·6)
Cough	141 (23·2)	2 (0·3)	105 (18·2)	1 (0·2)
Nausea	108 (17·7)	4 (0·7)	131 (22·7)	2 (0·3)
Diarrhoea	94 (15·4)	4 (0·7)	141 (24·4)	11 (1·9)
Asthenia	116 (19·0)	8 (1·3)	114 (19·7)	13 (2·2)
Dyspnoea	118 (19·4)	15 (2·5)	112 (19·4)	14 (2·4)
Anaemia	70 (11·5)	14 (2·3)	136 (23·5)	33 (5·7)
Alopecia	3 (0·5)	0	202 (34·9)	1 (0·2)
Constipation	107 (17·6)	2 (0·3)	82 (14·2)	1 (0·2)
Pyrexia	108 (17·7)	1 (0·2)	76 (13·1)	1 (0·2)
Peripheral oedema	54 (8·9)	1 (0·2)	82 (14·2)	3 (0·5)
Vomiting	74 (12·2)	2 (0·3)	62 (10·7)	4 (0·7)
Arthralgia	73 (12·0)	3 (0·5)	58 (10·0)	1 (0·2)
Myalgia	39 (6·4)	1 (0·2)	91 (15·7)	4 (0·7)
Back pain	67 (11·0)	7 (1·1)	42 (7·3)	4 (0·7)
Neutropenia	10 (1·6)	3 (0·5)	90 (15·6)	75 (13·0)
Peripheral neuropathy	24 (3·9)	0	65 (11·2)	7 (1·2)
Musculoskeletal pain	64 (10·5)	4 (0·7)	25 (4·3)	1 (0·2)
Stomatitis	19 (3·1)	1 (0·2)	63 (10·9)	11 (1·9)
Dysgeusia	18 (3·0)	0	58 (10·0)	0
Febrile neutropenia	1 (0·2)	1 (0·2)	62 (10·7)	62 (10·7)

Data are n (%), unless otherwise indicated.

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## References

- 1 Morrissey, K. M., M. Marchand, H. Patel, et al. 2019. "Alternative dosing regimens for atezolizumab: an example of model-informed drug development in the postmarketing setting." *Cancer Chemother Pharmacol* 84(6):1257-1267.
- 2 Rittmeyer, A., F. Barlesi, D. Waterkamp, et al. 2017. "Atezolizumab versus docetaxel in patients with previously treated non-small-cell lung cancer (OAK): a phase 3, open-label, multicentre randomised controlled trial." *Lancet* 389(10066):255-265.
- 3 Rittmeyer A, Barlesi F, Waterkamp D, et al. 2016 "Supplement to: Atezolizumab versus docetaxel in patients with previously treated non-small-cell lung cancer (OAK): a phase 3, open-label, multicentre randomised controlled trial." *Lancet*; published online Dec 12. [http://dx.doi.org/10.1016/S0140-6736\(16\)32517-X](http://dx.doi.org/10.1016/S0140-6736(16)32517-X).

## History

### Version 4

Date	Summary of changes
13/04/2022	<p>Protocol updated based on the consensus gained at the immunotherapy reference committee meeting held on 4<sup>th</sup> of March 2022. The following changes have been made across all immune checkpoint inhibitor protocols:</p> <ul style="list-style-type: none"> <li>• Clinical information- general irAEs, hepatitis and HIV, and fertility blocks updated. Individual irAE-related blocks removed. New block (baseline investigations) added.</li> <li>• Patient information- pregnancy and breastfeeding block in general advice section updated.</li> </ul> <p>Version number increased to V.4.</p>
20/05/2022	Protocol reviewed electronically by Medical Oncology Reference Committee. No change. Next review in 2 years.
20/09/2022	Blood tests in clinical information section updated to remove information about CTLA-4 containing regimens.

### Version 3

Date	Summary of changes
12/11/2020	<p>Protocol updated to align with ID 1993 Management of immune-related adverse events (irAEs) clinical resource which has been electronically reviewed and approved by the eviQ immunotherapy reference committee. The following changes have been made across all immune checkpoint inhibitor protocols:</p> <ul style="list-style-type: none"> <li>• Clinical information- cardiotoxicity, haematological toxicity, musculoskeletal toxicity and ocular toxicity added; rheumatological toxicity removed; immunotherapy clinical information changed to alphabetical order.</li> <li>• Side effects- haematological added; rheumatological replaced with musculoskeletal; immunotherapy side effects changed to alphabetical order.</li> </ul> <p>Arthralgia and myalgia non-irAE side effect removed to align with other immune checkpoint inhibitor protocols.</p> <p>Version number increased to V.3.</p>

## Version 2

Date	Summary of changes
10/09/2020	Patient information title updated- 'locally advanced or metastatic' added. Version number changed to V.2.

## Version 1

Date	Summary of changes
23/11/2018	New protocol taken to Medical Oncology Reference Committee meeting.
14/01/2019	Protocol approved and published. Review 1 year.
06/04/2020	Protocol reviewed electronically by Medical Oncology Reference Committee. Alternative dosing schedule of 1680 mg every 28 days added. Review 2 years.
15/05/2020	Premedication clinical information removed.

The information contained in this protocol is based on the highest level of available evidence and consensus of the eviQ reference committee regarding their views of currently accepted approaches to treatment. Any clinician (medical oncologist, haematologist, radiation oncologist, medical physicist, radiation therapist, pharmacist or nurse) seeking to apply or consult this protocol is expected to use independent clinical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. While eviQ endeavours to link to reliable sources that provide accurate information, eviQ and the Cancer Institute NSW do not endorse or accept responsibility for the accuracy, currency, reliability or correctness of the content of linked external information sources. Use is subject to eviQ's disclaimer available at [www.eviq.org.au](http://www.eviq.org.au)

**First approved:** 23 November 2018

**Last reviewed:** 20 May 2022

**Review due:** 30 June 2024

***The currency of this information is guaranteed only up until the date of printing, for any updates please check:***

<https://www.eviq.org.au/p/3408>

08 Aug 2023

# Patient information - Lung cancer locally advanced or metastatic - Atezolizumab

Patient's name:

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## Your treatment

It is important to understand that atezolizumab is not a traditional chemotherapy drug and has a different way of working. It is an immunotherapy treatment (also called anticancer drug) that works with your immune system to detect and destroy cancer cells. Immunotherapy can potentially affect any organ of the body.

The treatment schedule below explains how the immunotherapy drug for this treatment is given.

### Atezolizumab

This treatment cycle is repeated every 21 days. It can also be repeated every 28 days at a higher dose. Your doctor will advise you of the number of treatments you will have.

Day	Treatment	How it is given	How long it takes
1	<b>Atezolizumab</b> ( <i>a-te-zoe-LIZ-ue-mab</i> )	By a drip into a vein	About 1 hour (cycle 1 may take 1.5 hours)

**Prior to your treatment** tell your doctor if you are taking any other medicines (e.g. corticosteroids, immunosuppressive therapy), have or ever had chronic liver infections e.g. hepatitis B (HBV) or C (HCV), human immunodeficiency virus (HIV) or an organ transplant.

## When to get help



**It is important that you tell your doctor or nurse immediately if you develop any of the symptoms listed below in the side effects section. If you can't contact your doctor or nurse, go to your nearest hospital Emergency Department for help.**

### Emergency contact details

Ask your doctor or nurse from your treating team who to contact if you have a problem

Daytime:.....

Night/weekend:.....

Other instructions:.....

.....

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**During your treatment immediately** tell the doctor or nurse looking after you if you get any of the following problems:

- leaking from the area where the drugs are being given
- pain, stinging, swelling or redness in the area where the drugs are being given
- a skin rash, itching, feeling short of breath, wheezing, fever, shivers, or feeling dizzy or unwell in any way (allergic reaction).

## Other information about your treatment

### Treatment delays

There may 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. Your doctor will explain if you need any delays to your treatment and the reason why.

### Blood tests and monitoring

You will need to have a blood test before you start treatment and regularly throughout your treatment. Your doctor or nurse will tell you when to have these blood tests.

### Other medications given during this treatment

- **Steroids:** you may be given some steroid tablets to help reduce immune-related side effects. Your doctor or nurse will tell you how and when to take the steroids. You may need to monitor your blood sugar levels closely while you are taking steroids. If you have diabetes, your diabetic medication may need to be adjusted because of the effects of steroids. Speak to your diabetes advisor.

## Side effects

Cancer treatments can cause damage to normal cells in your body, which can cause side effects. Everyone gets different side effects, and some people will have more problems than others.

The table below shows some of the side effects you may get with this treatment. You are unlikely to get all of those listed and you may also get some side effects that have not been listed.

Tell your doctor or nurse about any side effects that worry you. Follow the instructions below and those given to you by your doctor or nurse.

Immunotherapy may cause serious immune reactions against your own body. These are called immune-related adverse events. They may occur during your treatment, or after your treatment has ended. Immunotherapy can affect many parts of your body. Some side effects can cause severe or life threatening conditions, so even mild side effects must be reported immediately. Do not try to treat these symptoms yourself without talking to your doctor or nurse first. You will be given an information pack at the start of your treatment. This contains an alert card which you should carry with you at all times. Bring this alert card with you to hospital, especially if you are unwell or attending the emergency department.

### Immune related side effects

#### Heart problems

- You may get:
  - chest pain or tightness
  - shortness of breath
  - swelling of your ankles
  - an abnormal heartbeat.
- Heart problems are uncommon but potentially fatal. If heart problems were to occur, symptoms usually start within the first 3 months of treatment, but can happen at any time even after the treatment has finished.
- Tell your doctor if you have a history of heart problems or high blood pressure.
- Before or during treatment, you may be asked to have a test to see how well your heart is working.
- **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the symptoms listed above.**

<b>Bowel and stomach inflammation</b>	<ul style="list-style-type: none"> <li>• You may get: <ul style="list-style-type: none"> <li>◦ bowel motions (stools, poo) that are more frequent or more liquid (diarrhoea)</li> <li>◦ blood or mucous in your stool</li> <li>◦ dark, tarry, or sticky bowel motions</li> <li>◦ bloating, cramping, pain or tenderness in your stomach area.</li> </ul> </li> <li>• Inform your doctor or nurse immediately if you get diarrhoea</li> <li>• Take your anti-diarrhoeal or steroid medication as directed by your doctor.</li> <li>• Drink plenty of fluids (unless you are on a fluid restriction).</li> <li>• Eat and drink small amounts more often.</li> <li>• Avoid spicy foods, dairy products, high fibre foods, and coffee.</li> <li>• <b>Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if your diarrhoea is not controlled despite taking anti-diarrhoea medicine, severe stomach pains and bloating, and/or if you feel dizzy or light-headed.</b></li> </ul>
<b>Blood problems</b>	<ul style="list-style-type: none"> <li>• Blood problems are infrequent but can be serious.</li> <li>• You may feel dizzy, light-headed, tired, weak and appear more pale than usual.</li> <li>• You may get: <ul style="list-style-type: none"> <li>• dark, tarry bowel motions (stools, poo)</li> <li>• blood in your urine or not urinating as often</li> <li>• dark-coloured urine</li> <li>• yellowing of the whites of your eyes, and/or your skin</li> <li>• pinpoint red spots on your skin</li> <li>• unexplained bleeding</li> <li>• major bruising</li> <li>• a fever</li> <li>• shortness of breath</li> <li>• a severe headache</li> <li>• confusion</li> <li>• faster heartbeat than normal</li> </ul> </li> <li>• <b>Tell your doctor or nurse immediately or go to the nearest hospital Emergency Department if it has been longer than 12 hours since you have emptied your bladder or if you get any of the symptoms listed above.</b></li> </ul>
<b>Liver damage</b>	<ul style="list-style-type: none"> <li>• You may get: <ul style="list-style-type: none"> <li>◦ fatigue</li> <li>◦ severe nausea and vomiting</li> <li>◦ weight loss</li> <li>◦ bruising or bleeding more easily</li> <li>◦ pain or tenderness on the right side of your stomach area</li> <li>◦ dark coloured urine</li> <li>◦ yellowing of the whites of your eyes and/or your skin</li> <li>◦ itchy skin</li> <li>◦ drowsiness</li> </ul> </li> <li>• You will have regular blood tests to check how well your liver is working.</li> <li>• Take your steroid medication as directed by your doctor.</li> <li>• <b>Tell your doctor or nurse as soon as possible if you notice that your urine is a dark colour, the whites of your eyes or skin look yellow, if you have unexplained bruising or bleeding or if you have severe stomach pain.</b></li> </ul>
<b>Muscle and joint problems</b>	<ul style="list-style-type: none"> <li>• You may get: <ul style="list-style-type: none"> <li>• muscle or joint stiffness, especially after a period of rest</li> <li>• muscle weakness</li> <li>• pain in your muscles or joints</li> <li>• joint swelling</li> <li>• tiredness</li> <li>• headaches</li> </ul> </li> <li>• Take your pain relief or steroid medication as directed by your doctor.</li> <li>• <b>Tell your doctor or nurse as soon as possible if you get any of the symptoms listed above.</b></li> </ul>

<p><b>Nervous system problems</b></p>	<ul style="list-style-type: none"> <li>• Nervous system changes are rare, but can be serious.</li> <li>• You may get: <ul style="list-style-type: none"> <li>◦ headaches</li> <li>◦ fever</li> <li>◦ stiff neck</li> <li>◦ confusion or difficulty concentrating</li> <li>◦ dizziness or drowsiness</li> <li>◦ loss of consciousness</li> <li>◦ muscle weakness or pain</li> <li>◦ numbness or tingling in your hands or feet</li> <li>◦ jerky movements.</li> </ul> </li> <li>• Take your steroid medication as directed by your doctor.</li> <li>• <b>Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the symptoms listed above.</b></li> </ul>
<p><b>Eye problems</b></p>	<ul style="list-style-type: none"> <li>• You may get: <ul style="list-style-type: none"> <li>◦ eye pain</li> <li>◦ itchy eyes</li> <li>◦ red or swollen eyes</li> <li>◦ blurred or change in vision</li> <li>◦ change in colour vision</li> <li>◦ watery or gritty eyes</li> <li>◦ dry eyes</li> <li>◦ sensitivity to light.</li> </ul> </li> <li>• Protect your eyes from the weather (sun and wind) by wearing sunglasses.</li> <li>• Use your eye drops or take your steroid medication as directed by your doctor.</li> <li>• <b>Tell your doctor or nurse as soon as possible if you get any of the symptoms listed above.</b></li> </ul>
<p><b>Hormone problems</b></p>	<ul style="list-style-type: none"> <li>• Hormone changes are infrequent, but can be serious.</li> <li>• You may get: <ul style="list-style-type: none"> <li>◦ headaches</li> <li>◦ tiredness, dizziness or fainting</li> <li>◦ abnormal heartbeat (faster than usual)</li> <li>◦ a feeling of being hot or cold more easily</li> <li>◦ excessive sweating</li> <li>◦ weight changes</li> <li>◦ a deepened voice</li> <li>◦ irregular or absent periods</li> <li>◦ nausea and vomiting</li> <li>◦ thirsty and need to urinate more often than normal</li> <li>◦ high blood sugar levels</li> <li>◦ pain in your stomach area</li> <li>◦ muscle pain or weakness</li> <li>◦ difficulty sleeping</li> <li>◦ agitated more easily</li> <li>◦ changes in your mood or behaviour, such as decreased sex drive or irritability.</li> </ul> </li> <li>• Take your hormone or steroid medication as directed by your doctor.</li> <li>• <b>Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you feel confused, weak, dizzy, or faint, or get sudden pain in your lower back or legs.</b></li> </ul>

<b>Lung problems</b>	<ul style="list-style-type: none"> <li>• You may get: <ul style="list-style-type: none"> <li>◦ shortness of breath</li> <li>◦ difficulty breathing</li> <li>◦ faster heartbeat than normal</li> <li>◦ chest pain</li> <li>◦ new or worsening cough</li> <li>◦ fever.</li> </ul> </li> <li>• Your doctor will monitor how well your lungs are working during your treatment.</li> <li>• Take your steroid medication as directed by your doctor.</li> <li>• <b>Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have chest pain or become short of breath.</b></li> </ul>
<b>Kidney damage</b>	<ul style="list-style-type: none"> <li>• This treatment can cause changes to how your kidneys work.</li> <li>• You may get: <ul style="list-style-type: none"> <li>◦ a feeling of needing to urinate less often than normal</li> <li>◦ blood in your urine</li> <li>◦ swollen hands and feet</li> <li>◦ loss of appetite.</li> </ul> </li> <li>• You will have regular blood tests to check how well your kidneys are working.</li> <li>• You may need to drink more fluids while you are having treatment. Your doctor or nurse will tell you if you need to do this.</li> <li>• Take your steroid medication as directed by your doctor.</li> <li>• <b>Tell your doctor or nurse as soon as possible if you notice that your urine changes colour or you don't need to empty your bladder as often.</b></li> </ul>
<b>Skin rash</b>	<ul style="list-style-type: none"> <li>• You may get <ul style="list-style-type: none"> <li>◦ a red rash</li> <li>◦ a bumpy rash</li> <li>◦ dry and itchy skin</li> <li>◦ skin peeling or blisters.</li> <li>◦ if you have had previous radiation therapy to an area this effect may be worse</li> </ul> </li> <li>• Moisturise your skin with a gentle non-perfumed moisturising cream like sorbolene or aqueous cream.</li> <li>• Avoid scratching your skin.</li> <li>• Avoid wearing tight fitting clothing</li> <li>• Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and sunscreen of SPF 50 or higher.</li> <li>• Take your antihistamine medication or apply your steroid cream as directed by your doctor.</li> <li>• <b>Tell your doctor or nurse as soon as possible if you notice any changes to the rash like pain or pus forming.</b></li> </ul>



## Thyroid problems

Thyroid problems are common with this treatment. The most common problem is an underactive thyroid gland (hypothyroidism), occasionally you may get an overactive thyroid gland (hyperthyroidism).

- If you have an **underactive** thyroid, you may get:
  - fatigue and low energy levels
  - depression
  - slow heart rate
  - unexplained weight gain
  - intolerance to cold temperatures
  - fatigued and aching muscles
  - dry, coarse skin
  - puffy face
  - hair loss
  - constipation
  - problems with concentration
  - changes in your periods
- If you have an **overactive** thyroid, you may get
  - abnormal heartbeat (faster than usual)
  - a feeling of being hot or cold more easily
  - excessive sweating
  - difficulty sleeping
  - anxiety, nervousness or agitated more easily
  - diarrhoea
  - changes in your periods
- You will have regular blood tests to check how well your thyroid is working.
- Take your hormone or steroid medication as directed by your doctor.
- Tell your doctor or nurse if you get any of the symptoms listed above.

## Non-immune related side effects

<b>Nausea and vomiting</b>	<ul style="list-style-type: none"><li>• You may feel sick (nausea) or be sick (vomit).</li><li>• Drink plenty of fluids (unless you are fluid restricted).</li><li>• Eat small meals more frequently.</li><li>• Try food that does not require much preparation.</li><li>• Try bland foods like dry biscuits or toast.</li><li>• Gentle exercise may help with nausea.</li><li>• Anti-sickness medication is usually not needed but may help in some people.</li><li>• Ask your doctor or nurse for eviQ patient information - <a href="#">Nausea and vomiting during cancer treatment</a>.</li><li>• <b>Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have uncontrolled vomiting or feel dizzy or light-headed.</b></li></ul>
<b>Tiredness and lack of energy (fatigue)</b>	<ul style="list-style-type: none"><li>• You may feel very tired, have no energy, sleep a lot, and not be able to do normal activities or things you enjoy.</li><li>• Do not drive or operate machinery if you are feeling tired.</li><li>• Nap for short periods (only 1 hour at a time)</li><li>• Prioritise your tasks to ensure the best use of your energy.</li><li>• Eat a well balanced diet and drink plenty of fluids (unless you are fluid restricted).</li><li>• Try some gentle exercise daily.</li><li>• Allow your friends and family to help.</li><li>• <b>Tell your doctor or nurse if you get any of the symptoms listed above.</b></li></ul>
<b>Fever</b>	<ul style="list-style-type: none"><li>• You may feel warm.</li><li>• Tell your doctor or nurse if you get this symptom.</li></ul>
<b>Flu-like symptoms</b>	<ul style="list-style-type: none"><li>• You may get:<ul style="list-style-type: none"><li>◦ a fever</li><li>◦ chills or sweats</li><li>◦ muscle and joint pain</li><li>◦ a cough</li><li>◦ headaches.</li></ul></li><li>• Tell your doctor or nurse if you get any of the symptoms listed above.</li><li>• <b>Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have a temperature of 38°C or higher.</b></li></ul>
<b>Appetite loss (anorexia)</b>	<ul style="list-style-type: none"><li>• You may not feel like eating.</li><li>• Try to avoid drinking fluids at meal times.</li><li>• Try to eat small meals or snacks regularly throughout the day.</li><li>• Try to eat food that is high in protein and calories.</li><li>• If you are worried about how much food you can eat, or if you are losing weight, ask to speak to a dietitian.</li></ul>

## 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 treatments.
- Don't stop or start any medications during treatment without talking to your doctor and pharmacist first.
- Paracetamol is safe to take if you have a headache or other mild aches and pains. It is recommended that you avoid taking

aspirin, ibuprofen and other anti-inflammatory type medications for pain while you are having treatment. However, if these medications have been prescribed by your doctor, do not stop taking them without speaking with your doctor.

- Don't have **any** vaccinations without talking to the doctor who is managing your cancer treatment.
- People you live with should be fully vaccinated, according to the current vaccination schedule. Extra care needs to be taken with hand washing and careful disposal of soiled nappies for infants who have recently received the rotavirus vaccine.

### **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.
- 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 get pregnant or 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.

### **Pregnancy and breastfeeding**

- Some cancer treatments can be dangerous to unborn babies. Talk to your doctor or nurse if you think there is any chance that you could be pregnant.
- Do not try to get pregnant or 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 pregnancy/fatherhood after completing this treatment, talk to your doctor. Some doctors advise waiting between 6 months and 2 years after treatment.
- Do not breastfeed if you are on this treatment, as anti-cancer medications can also pass into breast milk.

### **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
- Call the Lung Foundation Australia on 1800 654 301

### **Lung cancer information**

- Lung Foundation Australia – [lungfoundation.com.au](http://lungfoundation.com.au)
- Lungevity – [lungevity.org](http://lungevity.org)



This document is a guide only and cannot cover every possible situation. The health professionals caring for you should always consider your individual situation when making decisions about your care. Contact your cancer clinic staff or doctor if you have any questions or concerns about your treatment, or you are having problems coping with side effects. While eviQ endeavours to link to reliable sources that provide accurate information, eviQ and the Cancer Institute NSW do not endorse or accept responsibility for the accuracy, currency, reliability or correctness of the content of linked external information sources. Use of this document is subject to eviQ's disclaimer available at [www.eviq.org.au](http://www.eviq.org.au)

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***The currency of this information is guaranteed only up until the date of printing, for any updates please check:***

*<https://www.eviq.org.au/pi/3408>*

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