

# Breast metastatic DOXOrubicin three weekly

ID: 48 v.5   **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](#).

## 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
DOXOrubicin	60 mg/m <sup>2</sup> *	IV	1

\*Doxorubicin dose can vary from 60 mg/m<sup>2</sup> to 75 mg/m<sup>2</sup>. It is the consensus of the reference committee that a starting dose of 60 mg/m<sup>2</sup> is more appropriate for this patient population unless fit or being treated in the first line.

**Frequency:** 21 days

**Cycles:** Continuous until disease progression or unacceptable toxicity (up to 6 cycles)

**Drug status:** Doxorubicin is on the [PBS general schedule](#)

**Cost:** ~ \$100 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		
Dexamethasone	8 mg (PO)	60 minutes before chemotherapy
Palonosetron	0.25 mg (IV bolus)	30 minutes before chemotherapy
DOXOrubicin	60 mg/m <sup>2</sup> (IV)	over 5 to 15 minutes *
Day 2 and 3		
Dexamethasone	8 mg (PO)	ONCE a day (or in divided doses) with or after food. Note: dexamethasone doses on day 2 and 3 may not be

Day 2 and 3		
		required and may be reduced or omitted at the clinicians discretion. **

\* Doxorubicin dose can vary from 60 mg/m<sup>2</sup> to 75 mg/m<sup>2</sup>. It is the consensus of the reference committee that a starting dose of 60 mg/m<sup>2</sup> is more appropriate for this patient population unless fit or being treated in the first line.

\*\* Link to [ID 7 Prevention of chemotherapy induced nausea and vomiting](#)

**Frequency:** 21 days

**Cycles:** Continuous until disease progression or unacceptable toxicity (up to 6 cycles)

## Indications and patient population

- Advanced or metastatic breast cancer.

## 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 MODERATE</b>	Suggested default antiemetics have been added to the treatment schedule, and may be substituted to reflect institutional policy. For patients with a prior episode of chemotherapy induced nausea or vomiting, a NK1 receptor antagonist is available on the PBS in combination with a 5HT <sub>3</sub> antagonist and steroid. Ensure that patients also have sufficient antiemetics for breakthrough emesis: Metoclopramide 10 mg three times a day when necessary (maximum of 30 mg/24 hours, up to 5 days) OR Prochlorperazine 10 mg PO every 6 hours when necessary. Read more about <a href="#">preventing anti-cancer therapy induced nausea and vomiting</a>
<b>Cumulative lifetime dose of anthracyclines</b>	Cumulative doses should take into account all previous anthracyclines received during a patient's lifetime (i.e. daunorubicin, doxorubicin, epirubicin, idarubicin and mitoxantrone). Criteria for reducing the total anthracycline cumulative lifetime dose include: <ul style="list-style-type: none"> <li>patient is elderly</li> <li>prior mediastinal radiation</li> <li>hypertensive cardiomegaly</li> <li>concurrent therapy with high dose cyclophosphamide and some other cytotoxic drugs (e.g. bleomycin, dacarbazine, dactinomycin, etoposide, melphalan, mitomycin and vincristine).</li> </ul> Baseline clinical assessments include echocardiogram (ECHO) or gated heart pool scan (GHPS) and electrocardiogram (ECG) evaluation. Patients with normal baseline cardiac function (left ventricular ejection fraction (LVEF) > 50%) and low risk patients require LVEF monitoring when greater than 70% of the anthracycline threshold is reached or if the patient displays symptoms of cardiac impairment. Post-treatment cardiac monitoring is recommended for patients who have received high levels of total cumulative doses of anthracyclines at the clinician's discretion. Read more about <a href="#">cardiac toxicity associated with anthracyclines</a>
<b>Blood tests</b>	FBC, EUC and LFTs at baseline and prior to each treatment. Nadir FBC cycle 1.
<b>Hepatitis B screening and prophylaxis</b>	Routine screening for HBsAg and anti-HBc is NOT usually recommended for patients receiving this treatment. Read more about <a href="#">hepatitis B screening and prophylaxis in cancer patients requiring cytotoxic and/or immunosuppressive therapy</a>

<b>Vaccinations</b>	<p>Live vaccines are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease.</p> <p>Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the <a href="#">Australian Immunisation Handbook</a>.</p> <p>Read more about <a href="#">COVID-19 vaccines and cancer</a>.</p>
<b>Fertility, pregnancy and lactation</b>	<p>Cancer treatment can have harmful effects on fertility and this should be discussed with all patients of reproductive potential prior to commencing treatment. There is a risk of foetal harm in pregnant women. A pregnancy test should be considered prior to initiating treatment 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. Effective contraception methods and adequate contraception timeframe should be discussed with all patients of reproductive potential. Possibility of infant risk should be discussed with breastfeeding patients.</p> <p>Read more about the <a href="#">effect of cancer treatment on fertility</a></p>

## 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 \(ADIKD\).](#)

**Note:** all dose reductions are calculated as a percentage of the starting dose.

Haematological toxicity	
ANC x 10 <sup>9</sup> /L (pre-treatment blood test)	
1.0 to less than 1.5	Refer to local institutional guidelines; it is the view of the expert clinicians that treatment should continue if patient is clinically well
0.5 to less than 1.0	Delay treatment until recovery
less than 0.5	Delay treatment until recovery and reduce doxorubicin by 25% for subsequent cycles
Febrile neutropenia	Delay treatment until recovery and reduce doxorubicin by 25% for subsequent cycles
Platelets x 10 <sup>9</sup> /L (pre-treatment blood test)	
75 to less than 100	The general recommendation is to delay, however if the patient is clinically well it may be appropriate to continue treatment; refer to treating team and/or local institutional guidelines
50 to less than 75	Delay treatment until recovery
less than 50	Delay treatment until recovery and reduce doxorubicin by 25% for subsequent cycles

## Renal impairment

No dose modifications necessary

## Hepatic impairment

### Hepatic dysfunction

Mild	Reduce doxorubicin by 25%
Moderate	Reduce doxorubicin by 50%
Severe	Omit doxorubicin

## Mucositis and stomatitis

Grade 2	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follows: 1 <sup>st</sup> occurrence: No dose reduction 2 <sup>nd</sup> occurrence: Reduce doxorubicin by 25% 3 <sup>rd</sup> occurrence: Reduce doxorubicin by 50% 4 <sup>th</sup> occurrence: Omit doxorubicin
Grade 3 or Grade 4	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follows: 1 <sup>st</sup> occurrence: Reduce doxorubicin by 50% 2 <sup>nd</sup> occurrence: Omit doxorubicin

## 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](#)

Doxorubicin		
	Interaction	Clinical management
<b>Cardiotoxic drugs (eg. bevacizumab, calcium channel blockers, propranolol, trastuzumab)</b>	Increased risk of doxorubicin-induced cardiotoxicity	Avoid combination or monitor closely for cardiotoxicity
<b>Cyclophosphamide</b>	Sensitises the heart to the cardiotoxic effects of doxorubicin; also, doxorubicin may exacerbate cyclophosphamide induced cystitis	Monitor closely for cardiotoxicity and ensure adequate prophylaxis for haemorrhagic cystitis when combination is used
<b>Glucosamine</b>	Reduced efficacy of doxorubicin (due to induction of glucose-regulated stress proteins resulting in decreased expression of topoisomerase II <i>in vitro</i> )	The clinical effect of glucosamine taken orally is unknown. Avoid combination or monitor for decreased clinical response to doxorubicin
<b>CYP2D6 inhibitors (e.g. SSRIs (esp. paroxetine), perhexiline, cinacalcet, doxepin, flecainide, quinine, terbinafine)</b>	Increased toxicity of doxorubicin possible due to reduced clearance	Monitor for doxorubicin toxicity
<b>CYP3A4 inhibitors (e.g. aprepitant, azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)</b>	Increased toxicity of doxorubicin possible due to reduced clearance	Monitor for doxorubicin toxicity
<b>CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)</b>	Reduced efficacy of doxorubicin possible due to increased clearance	Monitor for decreased clinical response to doxorubicin

General		
	Interaction	Clinical management
<b>Warfarin</b>	Anti-cancer drugs may alter the anticoagulant effect of warfarin.	Monitor INR regularly and adjust warfarin dosage as appropriate; consider alternative anticoagulant.
<b>Direct oral anticoagulants (DOACs) e.g. apixaban, rivaroxaban, dabigatran</b>	<p>Interaction with both CYP3A4 and P-gp inhibitors /inducers.</p> <p>DOAC and anti-cancer drug levels may both be altered, possibly leading to loss of efficacy or toxicity (i.e. increased bleeding).</p>	<p>Apixaban: avoid concurrent use with strong <a href="#">CYP3A4</a> and <a href="#">P-gp</a> inhibitors. If treating VTE, avoid use with strong <a href="#">CYP3A4</a> and <a href="#">P-gp</a> inducers.</p> <p>Rivaroxaban: avoid concurrent use with strong <a href="#">CYP3A4</a> and <a href="#">P-gp</a> inhibitors.</p> <p>Dabigatran: avoid combination with strong <a href="#">P-gp</a> inducers and inhibitors.</p> <p>If concurrent use is unavoidable, monitor closely for efficacy/toxicity of both drugs.</p>
<b>Digoxin</b>	Anti-cancer drugs can damage the lining of the intestine; affecting the absorption of digoxin.	Monitor digoxin serum levels; adjust digoxin dosage as appropriate.
<b>Antiepileptics</b>	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.
<b>Antiplatelet agents and NSAIDs</b>	Increased risk of bleeding due to treatment related thrombocytopenia.	Avoid or minimise combination. If combination deemed essential, (e.g. low dose aspirin for ischaemic heart disease) monitor for signs of bleeding.
<b>Serotonergic drugs, including selective serotonin reuptake inhibitors (SSRIs e.g. paroxetine) and serotonin noradrenaline reuptake inhibitors (SNRIs e.g. venlafaxine)</b>	Increased risk of serotonin syndrome with concurrent use of 5-HT <sub>3</sub> receptor antagonists (e.g. palonosetron, ondansetron, granisetron, tropisetron, dolasetron, etc.)	<p>Avoid combination.</p> <p>If combination is clinically warranted, monitor for signs and symptoms of serotonin syndrome (e.g. confusion, agitation, tachycardia, hyperreflexia).</p> <p>For more information link to <a href="#">TGA Medicines Safety Update</a></p>
<b>Vaccines</b>	Diminished response to vaccines and increased risk of infection with live vaccines.	<p>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.</p> <p>For more information; refer to the recommended schedule of vaccination for cancer patients, as outlined in the <a href="#">Australian Immunisation Handbook</a></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*

## Day 1

**Approximate treatment time: 30 to 60 minutes.**

[Safe handling and waste management](#)

[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.

Prime IV line(s).

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

### Pre treatment medication

Verify dexamethasone taken or administer as prescribed.

Verify antiemetics taken or administer as prescribed.

## Chemotherapy - Time out

### Doxorubicin

**Administer doxorubicin (vesicant):**

- over 5 to 15 minutes
  - via a minibag **OR**
  - by IV bolus via a side port of a freely flowing IV infusion
- ensure vein is patent and monitor for signs of extravasation throughout administration
- flush with ~150 mL of sodium chloride 0.9%
- potential for flare reaction during administration of doxorubicin (facial flushing and red streaking along the vein) stop infusion and exclude extravasation before continuing at a slower rate of infusion.

Although rare, cardiac arrhythmias may occur during or immediately after doxorubicin administration. If sudden onset of dyspnoea, palpitations or irregular pulse occurs, stop administration immediately and obtain urgent medical officer review.

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

**Continue [safe handling](#) precautions until 7 days after completion of drug(s)**

## Discharge information

### Antiemetics

- Antiemetics as prescribed.

### 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)	
<b>Extravasation, tissue or vein injury</b>	The unintentional instillation or leakage of a drug or substance out of a blood vessel into surrounding tissue. This has the potential to cause damage to affected tissue. Read more about <a href="#">extravasation management</a>
<b>Flare reaction</b>	Anthracycline flare reaction is caused by a localised allergic reaction. It is characterised by erythematous vein streaking, urticaria and pruritus which may occur during drug administration and is often associated with too rapid an infusion. Extravasation must be ruled out if flare occurs.
<b>Nausea and vomiting</b>	Read more about <a href="#">prevention of treatment induced nausea and vomiting</a>
<b>Red-orange discolouration of urine</b>	Pink/red/orange discolouration of the urine. This can last for up to 48 hours after some anthracycline drugs.
<b>Taste and smell alteration</b>	Read more about <a href="#">taste and smell changes</a>
Early (onset days to weeks)	
<b>Neutropenia</b>	Abnormally low levels of neutrophils in the blood. This increases the risk of infection. Any fever or suspicion of infection should be investigated immediately and managed aggressively. Read more about <a href="#">immediate management of neutropenic fever</a>
<b>Thrombocytopenia</b>	A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding.  Read more about <a href="#">thrombocytopenia</a>
<b>Oral mucositis</b>	Erythematous and ulcerative lesions of the gastrointestinal tract (GIT). It commonly develops following chemotherapy, radiation therapy to the head, neck or oesophagus, and high dose chemotherapy followed by a blood and marrow transplant (BMT). Read more about <a href="#">oral mucositis</a>
<b>Fatigue</b>	Read more about <a href="#">fatigue</a>
<b>Photosensitivity</b>	Increased sensitivity to ultraviolet (UV) light resulting in an exaggerated sunburn-like reaction accompanied by stinging sensations and urticaria.
<b>Radiation recall</b>	Erythematous or inflammatory skin reaction resembling severe sunburn at sites previously treated with radiation therapy can occur with certain anti-cancer drugs. Symptoms include vesiculation, desquamation and ulceration of the skin. Read more about <a href="#">radiation recall</a>
Late (onset weeks to months)	
<b>Anaemia</b>	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about <a href="#">anaemia</a>
<b>Alopecia</b>	Hair loss may occur from all parts of the body. Patients can also experience mild to moderate discomfort of the hair follicles, and rarely pain as the hair is falling out. Read more about <a href="#">alopecia</a>
<b>Hyperpigmentation</b>	Darkening of an area of skin caused by the overproduction of melanin.
<b>Nail changes</b>	Hyperpigmentation, paronychia, onycholysis, splinter haemorrhage, pyogenic granuloma formation, subungal haematoma and subungal hyperkeratosis are some of the nail changes associated with anti-cancer drugs. Read more about <a href="#">nail toxicities</a>



## Delayed (onset months to years)

### Cardiotoxicity

Anthracyclines are the most frequently implicated anti-cancer drugs associated with cardiotoxicity, which typically manifests as a reduction in left ventricular ejection fraction (LVEF), cardiomyopathy, or symptomatic CHF. Anthracycline induced cardiotoxicity has been categorised into acute, early-onset chronic progressive and late-onset chronic progressive and is usually not reversible. The risk of clinical cardiotoxicity increases with a number of risk factors including higher total cumulative doses.

Read more about [cardiac toxicity associated with anthracyclines](#)

## Evidence

Doxorubicin monotherapy has been studied in advanced breast cancer at doses ranging from 60 mg/m<sup>2</sup> to 75 mg/m<sup>2</sup>.<sup>1, 2, 3</sup> Indirect comparisons between trials are difficult because of different patient population and trial designs. There are currently no published RCT comparing the dose of doxorubicin 60 mg/m<sup>2</sup> and 75 mg/m<sup>2</sup> in advanced breast cancer. As there is no evidence of inferiority of using doxorubicin 60mg/m<sup>2</sup>, it is the consensus of the reference committee that a starting dose of 60 mg/m<sup>2</sup> is more appropriate for this patient population.

The evidence supporting the use of first line single agent doxorubicin in advanced breast cancer comes from a phase III randomised controlled trial conducted by the European Organisation for Research and Treatment of Cancer (EORTC) group.<sup>1</sup>

Between August 1993 and May 1996, a total of 331 patients were enrolled. 166 patients were randomised to receive paclitaxel 200 mg/m<sup>2</sup> every 3 weeks and 165 patients were randomised to receive doxorubicin 75 mg/m<sup>2</sup> every 3 weeks. 7 courses were planned unless progression or unacceptable toxicity before the 7 courses were finished. Patients who progressed within the 7 courses underwent early cross-over to the alternative drug while a delayed cross-over was optional for the remainder of patients.

All patients were anthracycline and taxane naive.

The primary end points of the study were progression-free survival (PFS) in first line therapy and response rate (RR) in second line therapy. The secondary end points were response rate (RR) in first line therapy, quality of life, and overall survival (OS).

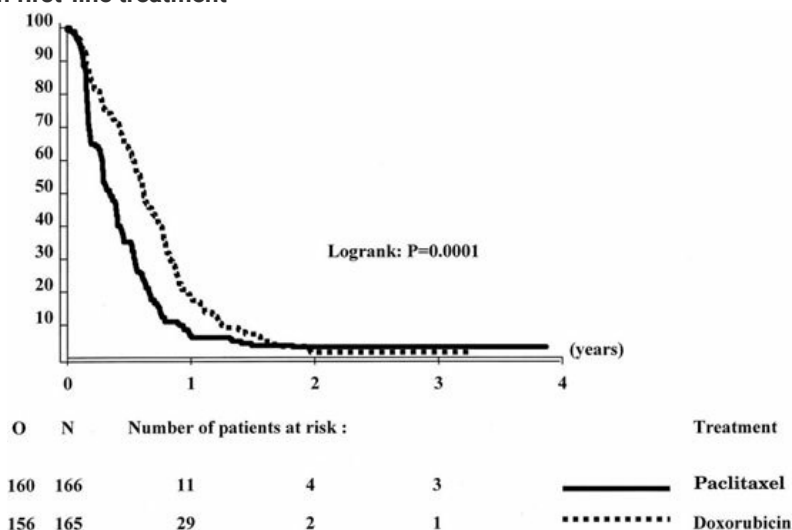
### Efficacy

As first line treatment, a median of 7 cycles was administered per patient in both arms. PFS in first-line therapy was significantly longer for doxorubicin than for paclitaxel (7.5 months vs 3.9 months respectively;  $p=0.0001$ ). The objective response rate (CR + PR) was also significantly better for doxorubicin than for paclitaxel in first-line treatment (41% vs 25% respectively;  $p=0.003$ ).

In second line therapy, cross-over to doxorubicin and to paclitaxel gave response rates of 30% and 16% respectively.

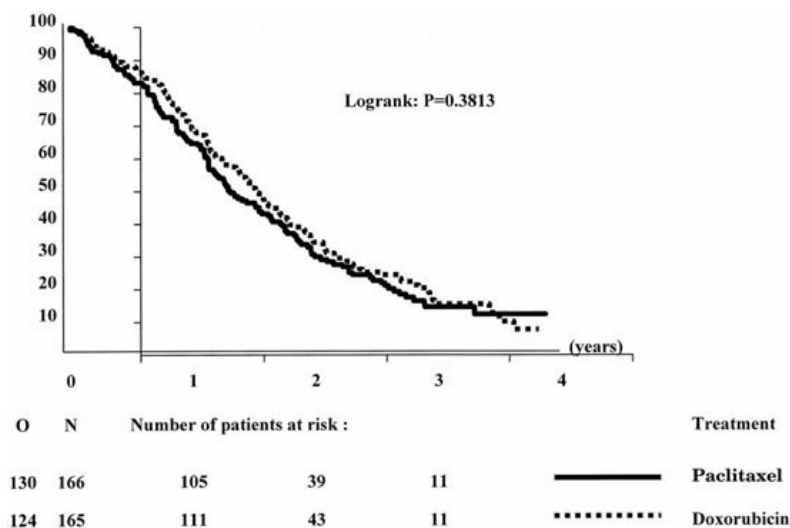
Overall, there was no significant difference in OS between the two study arms ( $p=0.38$ ), with a median survival of 18.3 months in the doxorubicin arm and 15.6 months in the paclitaxel arm. The cross-over design of the study may reduce the likelihood of observing such a difference.

### Progression-free survival on first-line treatment<sup>1</sup>



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## Overall survival<sup>1</sup>



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## Toxicity

Doxorubicin was more toxic than paclitaxel in terms of haematologic, gastrointestinal and cardiac side effects. In contrast, paclitaxel elicited more neurotoxicity (mainly sensory) and arthralgia/myalgia. 6 toxic deaths were encountered: 3 after doxorubicin as first-line therapy; 2 after doxorubicin as second-line therapy and 1 after paclitaxel in second-line treatment.

Regarding cardiotoxicity, a total of 12 patients (6 on first-line doxorubicin, 2 on second-line paclitaxel and 4 on second-line doxorubicin) developed congestive heart failure. The median cumulative dose of doxorubicin was 480 mg/m<sup>2</sup>.

An average of 93% and 99% of the planned dose intensities were reached in the doxorubicin and paclitaxel arms respectively.

In terms of QOL, there was no difference reported between groups. A detailed analysis showed that the greater toxicity of doxorubicin was compensated by better pain control than that achieved with paclitaxel.<sup>4</sup>

## Toxicities observed during first- and second-line treatment<sup>1</sup>

Table 5. Main Clinically Relevant Adverse Events and Grade 3 to 4 NCI CTC Toxicity Observed Per Patient During First-Line Treatment

Toxicity	Patients Treated With Paclitaxel (n = 164)		Patients Treated With Doxorubicin (n = 163)		P
	No.	%	No.	%	
Neutropenia grade 4	66	40	139	85	<.001
Febrile neutropenia	11	7	33	20	<.001
Documented infection	6	4	10	6	.319
Vomiting	4	2	22	13	<.001
Stomatitis	2	1	25	15	<.001
Arthralgia/myalgia	7	4	0	0	.015
Sensory neurotoxicity	14	9	0	0	<.001
CHF	0	0	6	4	.015
Myocardial infarction	1	1	2	2	.62
Hospitalization (any cause)	46	28	61	37	.07
Toxic death	0	0	3	3	.123

Abbreviation: CHF, congestive heart failure.

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**Table 6. Main Clinically Relevant Adverse Events and Grade 3 to 4 NCI CTC Toxicity Observed Per Patient During Second-Line Treatment**

Toxicity	Patients Treated With Paclitaxel (n = 77)		Patients Treated With Doxorubicin (n = 91)	
	No.	%	No.	%
Neutropenia grade 4	35	45	70	77
Febrile neutropenia	6	8	18	20
Documented infection	4	5	3	3
Vomiting	2	3	9	10
Stomatitis	3	4	7	8
Arthralgia/myalgia	4	5	0	0
Sensory neurotoxicity	8	10	1	1
CHF	2	3	4	4
Toxic death	1	1	2	2

Abbreviation: CHF, congestive heart failure.

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## References

- 1 Paridaens, R., L. Biganzoli, P. Bruning, et al. 2000. "Paclitaxel versus doxorubicin as first-line single-agent chemotherapy for metastatic breast cancer: a European Organization for Research and Treatment of Cancer Randomized Study with cross-over." *J Clin Oncol* 18(4):724-733.
- 2 Chan, S., K. Friedrichs, D. Noel, et al. 1999. "Prospective randomized trial of docetaxel versus doxorubicin in patients with metastatic breast cancer." *J Clin Oncol* 17(8):2341-2354.
- 3 Sledge, G. W., D. Neuberg, P. Bernardo, et al. 2003. "Phase III trial of doxorubicin, paclitaxel, and the combination of doxorubicin and paclitaxel as front-line chemotherapy for metastatic breast cancer: an intergroup trial (E1193)." *J.Clin Oncol* 21(4):588-592.
- 4 Kramer, J. A., D. Curran, M. Piccart, et al. 2000. "Randomised trial of paclitaxel versus doxorubicin as first-line chemotherapy for advanced breast cancer: quality of life evaluation using the EORTC QLQ-C30 and the Rotterdam symptom checklist." *Eur J Cancer* 36(12):1488-1497.

## History

### Version 5

Date	Summary of changes
03/08/2009	Reviewed and transferred to eviQ.
28/06/2010	Haematological dose modifications updated (20% changed to 25% dose reduction).
26/10/2010	Dose modifications updated: "consider reducing" changed to "reduce".
11/01/2011	New format to allow for export of protocol information. Protocol version number changed to V.2. Antiemetics and premedications added to the treatment schedule. Additional Clinical Information, Key Prescribing table and Key Administration table combined into new section titled Clinical Considerations. Drug specific information placed behind the drug name link.
18/04/2012	Palonosetron added as the preferred 5HT <sub>3</sub> antagonist for moderate emetogenicity.
27/04/2012	Protocol reviewed at Medical Oncology Reference Committee meeting. Consensus to reduce doxorubicin dose to 60 mg/m <sup>2</sup> (was 75 mg/m <sup>2</sup> ) as more appropriate for this patient population.

Date	Summary of changes
	Evidence reviewed and updated to include explanation for dose change. Next review in 2 years.
09/05/2014	Protocol reviewed by email survey. No change and next review in 2 years. PHC view removed.
18/02/2016	Discussion with Medical Oncology Reference Committee Chairs and protocol to be reviewed every 5 years. Next review due in 3 years.
10/10/2016	Treatment time updated to 30-60 minutes.
31/05/2017	Transferred to new eviQ website. Protocol version number changed to V.4. Protocol title updated: "three weekly" added.  Hepatitis B screening changed to NOT recommended.
10/05/2018	Haematological dose modifications updated as per consensus of the expert clinician group. Version number changed to V.5.
22/06/2018	Antiemetics updated to be in line with international guidelines. Note to dexamethasone added.
23/09/2019	Protocol reviewed at Medical Oncology Reference Committee meeting on 30/08/2019. No changes. Next review in 5 years.

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)

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**Review due:** 31 December 2024

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<https://www.eviq.org.au/p/48>

07 Jun 2023

# Patient information - Breast cancer metastatic - Doxorubicin three weekly

Patient's name:

## Your treatment

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


### Doxorubicin

This treatment cycle is repeated every 21 days. 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>Doxorubicin</b> ( <i>dox-oh-roo-bi-sin</i> )	By a drip into a vein	About 30 minutes to 1 hour

## 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 become unwell.

 <b>IMMEDIATELY go to your nearest hospital Emergency Department, or contact your doctor or nurse if you have any of the following at any time:</b>	<b>Emergency contact details</b> Ask your doctor or nurse from your treating team who to contact if you have a problem
<ul style="list-style-type: none"><li>• a temperature of 38°C or higher</li><li>• chills, sweats, shivers or shakes</li><li>• shortness of breath</li><li>• uncontrolled vomiting or diarrhoea</li><li>• pain, tingling or discomfort in your chest or arms</li><li>• you become unwell.</li></ul>	Daytime:..... Night/weekend:..... Other instructions:..... ..... ..... .....

**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 or at any injection sites
- 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

### 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

Anti-cancer drugs can reduce the number of blood cells in your body. You will need to have regular blood tests to check that your blood cell count has returned to normal. If your blood count is low, your treatment may be delayed until it has returned to normal. Your doctor or nurse will tell you when to have these blood tests.

## Other medications given during this treatment

- **Anti-sickness (anti-nausea) medication:** you may be given some anti-sickness medication. Make sure you take this medication as your doctor or nurse tells you, even if you don't feel sick. This can help to prevent the sickness starting.

## 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.

Immediate (onset hours to days)	
<b>Pain or swelling at injection site (extravasation)</b>	<ul style="list-style-type: none"><li>• This treatment can cause serious injury if it leaks from the area where it is going into the vein.</li><li>• This can cause pain, stinging, swelling or redness at or near the site where the drug enters the vein.</li><li>• If not treated correctly, you may get blistering and ulceration.</li><li>• <b>Tell your doctor or nurse immediately if you get any of the symptoms listed above during or after treatment.</b></li></ul>
<b>Redness and itching along vein</b>	<ul style="list-style-type: none"><li>• You may get redness and itching along the vein where your chemotherapy is being infused.</li><li>• This will usually go away within 30 minutes of stopping the injection.</li><li>• <b>Tell your doctor or nurse as soon as possible if you get any of the symptoms listed above. Your nurse will check to make sure the drug has not leaked out of the vein.</b></li></ul>
<b>Nausea and vomiting</b>	<ul style="list-style-type: none"><li>• You may feel sick (nausea) or be sick (vomit).</li><li>• Take your anti-sickness medication as directed even if you don't feel sick.</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>• 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>Urine turning orange or red</b>	<ul style="list-style-type: none"><li>• Your urine will turn an orange or red colour.</li><li>• This is not harmful and should only last for up to 48 hours after treatment.</li></ul>
<b>Taste and smell changes</b>	<ul style="list-style-type: none"><li>• You may find that food loses its taste or tastes different.</li><li>• These changes are likely to go away with time.</li><li>• Do your mouth care regularly.</li><li>• Chew on sugar-free gum or eat sugar-free mints.</li><li>• Add flavour to your food with sauces and herbs.</li><li>• Ask your doctor or nurse for eviQ patient information - <a href="#">Taste and smell changes during cancer treatment</a>.</li></ul>

Early (onset days to weeks)	
<b>Infection risk (neutropenia)</b>	<ul style="list-style-type: none"> <li>• This treatment lowers the amount of white blood cells in your body. The type of white blood cells that help to fight infection are called neutrophils. Having low level of neutrophils is called neutropenia. If you have neutropenia, you are at greater risk of getting an infection. It also means that your body can't fight infections as well as usual. This is a serious side effect, and can be life threatening.</li> <li>• Wash your hands often.</li> <li>• Keep a thermometer at home and take your temperature regularly, and if you feel unwell.</li> <li>• Do your mouth care regularly.</li> <li>• Inspect your central line site (if you have one) daily for any redness, pus or swelling.</li> <li>• Limit contact with people who are sick.</li> <li>• Learn how to recognise the signs of infection.</li> <li>• Ask your doctor or nurse for eviQ patient information - <a href="#">Infection during cancer treatment</a>.</li> <li>• <b>Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms:</b> <ul style="list-style-type: none"> <li>◦ a temperature of 38°C or higher</li> <li>◦ chills, shivers, sweats or shakes</li> <li>◦ a sore throat or cough</li> <li>◦ uncontrolled diarrhoea</li> <li>◦ shortness of breath</li> <li>◦ a fast heartbeat</li> <li>◦ become unwell even without a temperature.</li> </ul> </li> </ul>
<b>Low platelets (thrombocytopenia)</b>	<ul style="list-style-type: none"> <li>• This treatment lowers the amount of platelets in your blood. Platelets help your blood to clot. When they are low, you are at an increased risk of bleeding and bruising.</li> <li>• Try not to bruise or cut yourself.</li> <li>• Avoid contact sport or vigorous exercise.</li> <li>• Clear your nose by blowing gently.</li> <li>• Avoid constipation.</li> <li>• Brush your teeth with a soft toothbrush.</li> <li>• Don't take aspirin, ibuprofen or other similar anti-inflammatory medications unless your doctor tells you to.</li> <li>• Tell your doctor or nurse if you have any bruising or bleeding.</li> <li>• <b>Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if you have any uncontrolled bleeding.</b></li> </ul>
<b>Mouth pain and soreness (mucositis)</b>	<ul style="list-style-type: none"> <li>• You may have: <ul style="list-style-type: none"> <li>◦ bleeding gums</li> <li>◦ mouth ulcers</li> <li>◦ a white coating on your tongue</li> <li>◦ pain in the mouth or throat</li> <li>◦ difficulty eating or swallowing.</li> </ul> </li> <li>• Avoid spicy, acidic or crunchy foods and very hot or cold food and drinks.</li> <li>• Try bland and soft foods.</li> <li>• Brush your teeth gently with a soft toothbrush after each meal and at bedtime. If you normally floss continue to do so.</li> <li>• Rinse your mouth after you eat and brush your teeth, using either: <ul style="list-style-type: none"> <li>◦ 1/4 teaspoon of salt in 1 cup of warm water, or</li> <li>◦ 1/4 teaspoon of bicarbonate of soda in 1 cup of warm water</li> </ul> </li> <li>• Ask your doctor or nurse for eviQ patient information - <a href="#">Mouth problems during cancer treatment</a>.</li> <li>• <b>Tell your doctor or nurse if you get any of the symptoms listed above.</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>Skin that is more sensitive to the sun (photosensitivity)</b>	<ul style="list-style-type: none"> <li>• After being out in the sun you may develop a rash like a bad sunburn.</li> <li>• Your skin may become red, swollen and blistered.</li> <li>• Avoid direct sunlight.</li> <li>• Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and a sunscreen of SPF 50 or higher.</li> <li>• <b>Tell your doctor or nurse if you get any of the symptoms listed above.</b></li> </ul>
<b>Skin reaction in an area previously treated with radiation therapy (radiation recall)</b>	<ul style="list-style-type: none"> <li>• In the area that was treated with radiation therapy, your skin may become: <ul style="list-style-type: none"> <li>◦ dry, red and itchy</li> <li>◦ tender and swollen</li> </ul> </li> <li>• It may also: <ul style="list-style-type: none"> <li>◦ peel or blister</li> <li>◦ form ulcers</li> </ul> </li> <li>• This usually happens weeks or months after chemotherapy treatment.</li> <li>• Avoid wearing tight clothing.</li> <li>• Avoid direct sunlight and very hot or cold temperatures.</li> <li>• Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and a sunscreen of SPF 50 or higher.</li> <li>• Tell your doctor or nurse if you get any of the symptoms listed above.</li> </ul>



Late (onset weeks to months)	
<b>Low red blood cells (anaemia)</b>	<ul style="list-style-type: none"> <li>You may feel dizzy, light-headed, tired and appear more pale than usual.</li> <li>Tell your doctor or nurse if you have any of these signs or symptoms. You might need a blood transfusion.</li> <li><b>Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have any chest pain, trouble breathing, or feel like your heart is racing.</b></li> </ul>
<b>Hair loss (alopecia)</b>	<ul style="list-style-type: none"> <li>Your hair may start to fall out from your head and body.</li> <li>Hair loss usually starts 2 to 3 weeks after your first treatment.</li> <li>You may become completely bald and your scalp might feel tender.</li> <li>Use a gentle shampoo and a soft brush.</li> <li>Take care with hair products like hairspray, hair dye, bleaches and perms.</li> <li>Protect your scalp from the cold with a hat, scarf or wig.</li> <li>Protect your scalp from the sun with a hat or sunscreen of SPF 50 or higher.</li> <li>Moisturise your scalp to prevent itching.</li> <li>Ask your doctor or nurse about the <a href="#">Look Good Feel Better</a> program</li> </ul>
<b>Skin colour changes</b>	<ul style="list-style-type: none"> <li>You may have darkening of your skin, especially in areas that are exposed to the sun.</li> <li>You may also notice darkening of your tongue, gums and over your finger joints.</li> <li>These skin changes may fade over time.</li> <li>Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and a sunscreen of SPF 50 or higher.</li> </ul>
<b>Nail changes</b>	<ul style="list-style-type: none"> <li>Your nails may: <ul style="list-style-type: none"> <li>grow more slowly</li> <li>become darker</li> <li>develop ridges or white lines</li> <li>become brittle and flaky</li> </ul> </li> <li>In some cases, you may lose your nails completely.</li> <li>Keep your nails clean and short.</li> <li>Avoid things like biting your fingernails, getting a manicure, pedicure or false nails.</li> <li>Wear gloves when you wash the dishes, work in the garden, or clean the house.</li> </ul>

Delayed (onset months to years)	
<b>Heart problems</b>	<ul style="list-style-type: none"> <li>You may get: <ul style="list-style-type: none"> <li>chest pain or tightness</li> <li>shortness of breath</li> <li>swelling of your ankles</li> <li>an abnormal heartbeat.</li> </ul> </li> <li>Heart problems can occur months to years after treatment.</li> <li>Tell your doctor if you have a history of heart problems or high blood pressure.</li> <li>Before or during treatment, you may be asked to have a test to see how well your heart is working.</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>

## General advice for people having cancer treatment

### Chemotherapy safety

- Learn how to keep you and your family safe while you are having anticancer drugs.
- See our patient information sheet - [Chemotherapy safety at home](#).

### 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.
- 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.
- Vaccinations such as flu and tetanus vaccines are safe to receive while having treatment. Do not have any live vaccines during your treatment or for 6 months after it finishes. If you are unsure, check with your doctor before you have any vaccinations.
- People you live with should be fully vaccinated, including having live vaccines 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.
- 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 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.

### **Risk of developing a second cancer**

- Some anticancer treatments can increase your chance of developing a second cancer, this is rare. Your doctor will discuss with you the specific risks of your treatment.

### **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.

Where to get more information

Telephone support

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

Breast cancer information

- Australasian Lymphology Association – [lymphoedema.org.au](http://lymphoedema.org.au)
- Australasian Menopause Society – [menopause.org.au](http://menopause.org.au)
- Breast Cancer Network Australia – [bcna.org.au](http://bcna.org.au)
- National Breast Cancer Foundation – [nbcf.org.au](http://nbcf.org.au)
- YWCA Encore breast cancer exercise program – [ywcaencore.org.au](http://ywcaencore.org.au)

General cancer information and support

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

Additional notes:

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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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