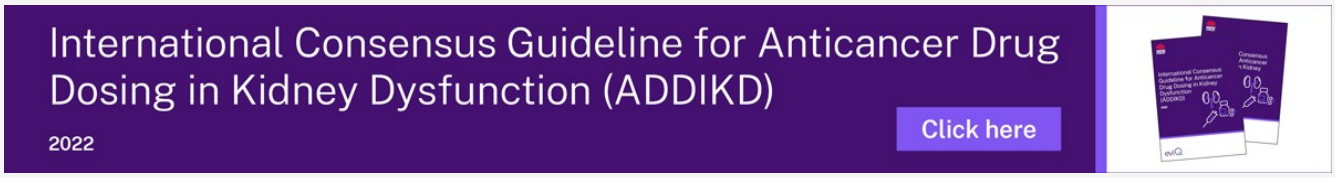
Breast metastatic DOXOrubicin pegylated liposomal

ID: 35 v.4 **Endorsed**

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.



Treatment schedule - Overview

Cycle 1 and further cycles

Drug	Dose	Route	Day
DOXOrubicin liposomal	40 mg/m^2 *	IV infusion	1

*It is the consensus of the reference committee that the original dose of liposomal doxorubicin (50 mg/m^2) used in the clinical trial be reduced to 40 mg/m^2 as the higher dose is undeliverable in clinical practice due to toxicity.

Frequency: 28 days

Cycles: Continuous until maximum improvement or unacceptable toxicity

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Drug status: Pegylated liposomal doxorubicin is PBS authority

Cost: ~ $830 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		
Metoclopramide	10 mg (PO)	one tablet when necessary (maximum of 30 mg/24 hours, up to 5 days)
DOXOrubicin liposomal	40 mg/m^2 (IV infusion)	in 250 mL glucose 5% at a rate no greater than 1 mg/min for the first cycle then over 60 minutes for subsequent cycles

- It is the consensus of the reference committee that the original dose of liposomal doxorubicin (50 mg/m^2) used in the clinical trial be reduced to 40 mg/m^2 as the higher dose is undeliverable in clinical practice due to toxicity.

Frequency: 28 days

Cycles: Continuous until maximum improvement or unacceptable toxicity

Indications and patient population

- Metastatic breast cancer
  - potentially anthracycline sensitive disease
  - patients at increased risk of cardiotoxicity.

Clinical information

Venous access required	IV cannula (IVC) or central venous access device (CVAD) is required to administer this treatment. Read more about central venous access device line selection
Hypersensitivity/infusion related reaction	High risk with pegylated liposomal doxorubicin.
Emetogenicity LOW	Suggested default antiemetics have been added to the treatment schedule, and may be substituted to reflect institutional policy. 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 preventing anti-cancer therapy induced nausea and vomiting
Cumulative lifetime dose of anthracyclines	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: • patient is elderly • prior mediastinal radiation • hypertensive cardiomegaly • concurrent therapy with high dose cyclophosphamide and some other cytotoxic drugs (e.g. bleomycin, dacarbazine, dactinomycin, etoposide, melphalan, mitomycin and vincristine). 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 cardiac toxicity associated with anthracyclines
Hand-foot syndrome	Monitor patient for presence of hand-foot syndrome (palmar-plantar erythrodysaesthesia). If present patient may require an interruption in treatment. For further information see *Dose modifications* section below. Read more about hand-food syndrome or palmar-plantar erythrodysaesthesia (PPE)
Blood tests	FBC, EUC and LFTs at baseline and prior to each treatment.
Hepatitis B screening and prophylaxis	Routine screening for HBsAg and anti-HBc is NOT usually recommended for patients receiving this treatment. Read more about hepatitis B screening and prophylaxis in cancer patients requiring cytotoxic and/or immunosuppressive therapy

Vaccinations	Live vaccines are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease. Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the Australian Immunisation Handbook. Read more about COVID-19 vaccines and cancer.
Fertility, pregnancy and lactation	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. Read more about the effect of cancer treatment on fertility

Dose modifications

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

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

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

Haematological toxicity	
ANC x 10^9/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 liposomal doxorubicin by 25% for subsequent cycles
Febrile neutropenia	Delay treatment until recovery and reduce liposomal doxorubicin by 25% for subsequent cycles
Platelets x 10^9/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 liposomal doxorubicin by 25% for subsequent

Haematological toxicity	
	cycles

Renal impairment
No dose modifications necessary

Hepatic impairment	
Hepatic dysfunction	
Mild	Reduce liposomal doxorubicin by 25%
Moderate	Reduce liposomal doxorubicin by 50%
Severe	Omit liposomal 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: 1st occurrence: No dose reduction 2nd occurrence: Reduce liposomal doxorubicin by 25% 3rd occurrence: Reduce liposomal doxorubicin by 50% 4th occurrence: Omit liposomal 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: 1st occurrence: Reduce liposomal doxorubicin by 50% 2nd occurrence: Omit liposomal doxorubicin

Hand foot syndrome (link to Hand foot syndrome (Palmar-plantar erythrodysaesthesia)	
Grade 2	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follows: 1st occurrence: No dose reduction 2nd occurrence: Reduce liposomal doxorubicin 25% 3rd occurrence: Reduce liposomal doxorubicin by 50% 4th occurrence: Omit liposomal doxorubicin
Grade 3	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follows: 1st occurrence: Reduce liposomal doxorubicin by 50% 2nd occurrence: Omit liposomal 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**
Cardiotoxic drugs (eg. bevacizumab, calcium channel blockers, propranolol, trastuzumab)	Increased risk of doxorubicin-induced cardiotoxicity	Avoid combination or monitor closely for cardiotoxicity
Cyclophosphamide	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
Glucosamine	Reduced efficacy of doxorubicin (due to induction of glucose-regulated stress proteins resulting in decreased expression of topoisomerase II *in vitro*)	The clinical effect of glucosamine taken orally is unknown. Avoid combination or monitor for decreased clinical response to doxorubicin
CYP2D6 inhibitors (e.g. SSRIs (esp. paroxetine), perhexiline, cinacalcet, doxepin, flecainide, quinine, terbinafine)	Increased toxicity of doxorubicin possible due to reduced clearance	Monitor for doxorubicin toxicity
CYP3A4 inhibitors (e.g. aprepitant, azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)	Increased toxicity of doxorubicin possible due to reduced clearance	Monitor for doxorubicin toxicity
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of doxorubicin possible due to increased clearance	Monitor for decreased clinical response to doxorubicin

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

Administration

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

product information monographs via the TGA website for further information.

Day 1

Approximate treatment time: 1 to 3 hours

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

Administer antiemetics if required

Chemotherapy - Time out

Liposomal doxorubicin

- liposomal doxorubicin is only compatible with glucose 5%.
- do not use with an in-line filter.

Initial infusion - administer liposomal doxorubicin (irritant with vesicant properties):

- via IV infusion at a rate no greater than 1 mg/min
- side lined with a concurrent glucose 5% infusion
- observe for hypersensitivity reaction
- flush with ~ 100 mL of glucose 5%.

Subsequent infusions:

- if previous hypersensitivity reaction, administer subsequent infusions following medical review at a slower rate and include premedication with an antihistamine and/or a corticosteroid
- if no previous hypersensitivity reaction administer via IV infusion over 60 minutes
- further dilution is recommended by a side line of glucose 5% to minimise the risk of thrombosis.

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)	
Hypersensitivity reaction	Anaphylaxis and infusion related reactions can occur with this treatment. Read more about hypersensitivity reaction
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting
Red-orange discolouration of urine	Pink/red/orange discolouration of the urine. This can last for up to 48 hours after some anthracycline drugs.
Taste and smell alteration	Read more about taste and smell changes

Early (onset days to weeks)	
Neutropenia	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 immediate management of neutropenic fever
Oral mucositis	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 oral mucositis
Fatigue	Read more about fatigue
Diarrhoea	Read more about treatment induced diarrhoea
Anorexia	Loss of appetite accompanied by decreased food intake. Read more about anorexia
Palmar-plantar erythrodysaesthesia (PPE) - hand-foot syndrome (HFS)	Bilateral erythema, tenderness, pain, swelling, tingling, numbness, pruritus, dry rash, or moist desquamation and ulceration of the palms and soles. It is also known as hand-foot syndrome (HFS). Symptoms appear to be dose dependent and palms are affected more than soles. Read more about hand-foot syndrome associated with chemotherapy
Radiation recall	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 radiation recall

Late (onset weeks to months)	
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia
Alopecia - partial	Hair thinning and/or patchy hair loss. Patients can also experience mild to moderate discomfort of the hair follicles, and rarely pain as the hair is falling out. Read more about alopecia
Cognitive changes (chemo fog)	Changes in cognition characterised by memory loss, forgetfulness and feeling vague. This is also referred to as 'chemo brain' or 'chemo fog'. Read more about cognitive changes (chemo fog)

Delayed (onset months to years)	
Menopausal symptoms	Irregular or absent periods, hot flushes, mood swings, sleep disturbance, night sweats, vaginal dryness, decreased libido and dyspareunia. This is caused by ovarian failure and may be temporary or permanent.
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

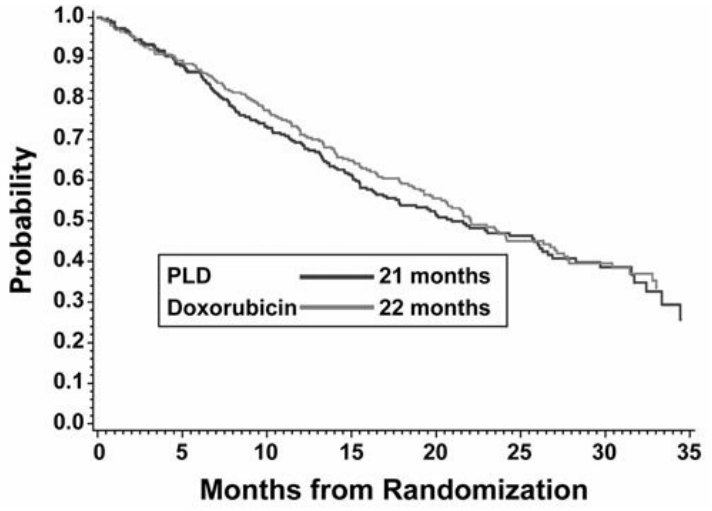
Liposomal doxorubicin at a dose of 50 mg/m^2 is equally effective as first line therapy of metastatic breast cancer as doxorubicin 60 mg/m^2 with the advantage of reduced cardiac toxicity.[1]Cardiac toxicity remains at < 10% with cumulative doses up to 600 mg/m^2 in anthracycline naive patients. However, It is important to note that liposomal doxorubicin is not effective in anthracycline resistant disease[2] and shows minimal activity in taxane refractory patients. A randomised controlled trial of liposomal doxorubicin compared to vinorelbine or mitomycin C and vinblastine, in women with taxane-refractory advanced breast cancer, showed minimal activity in either arm with an 8-10% response rate.[3]

Efficacy

	Liposomal Doxorubicin	Doxorubicin
Response rate	33%	38%
Median duration of response	7.3 months	7.1 months
Overall survival	21 months	22 months

Liposomal doxorubicin provides comparable efficacy to doxorubicin with significantly less cardiac toxicity than doxorubicin, myelosuppression, vomiting and alopecia.[1]

Overall survival [1]



[HR = 0.94 (95% CI for HR 0.74 - 1.19)]

Toxicity

In both groups 24% of patients discontinued due to toxicity (adverse event or cardiac toxicity). In the liposomal doxorubicin group 22% discontinued due to an adverse event and 2.4% due to cardiac toxicity, whereas among the doxorubicin group 9.4% discontinued due to an adverse event and 14% due to cardiac toxicity. Palmar-plantar erythrodysesthesia (PPE) was the most common adverse event 48% (grade 3 = 17%) with the liposomal doxorubicin group.[1]

Treatment-related adverse events[1]

Table 6. Treatment-related adverse events (>5%)

All adverse events	No. of patients (%)					
	PLD (n = 254)			Doxorubicin (n = 255)		
	All Grades	Grades 3/4		All Grades	Grades 3/4	
	215 (85)	111 (44)		218 (85)	69 (27)	
	All Grades	Grade 3	Grade 4	All Grades	Grade 3	Grade 4
Non-hematological						
PPE	123 (48)	42 (17)	0	5 (2)	0	0
Nausea	94 (37)	8 (3)	0	136 (53)	12 (5)	0
Mucositis	59 (23)	10 (4)	0	33 (13)	5 (2)	0
Stomatitis	55 (22)	12 (5)	0	38 (15)	4 (2)	0
Alopecia	51 (20)	0	0	169 (66)	0	0
Vomiting	48 (19)	2 (<1)	0	78 (31)	11 (4)	0
Fatigue	31 (12)	2 (<1)	0	40 (16)	4 (2)	0
Anorexia	27 (11)	3 (1)	0	26 (10)	1 (<1)	0
Asthenia	26 (10)	3 (1)	0	32 (13)	3 (1)	0
Rash	25 (10)	6 (2)	0	4 (2)	0	0
Abdominal pain	21 (8)	3 (1)	0	11 (4)	3 (1)	0
Constipation	21 (8)	2 (<1)	0	24 (9)	1 (<1)	0
Pigmentation abnormal	21 (8)	1 (<1)	0	6 (2)	1 (<1)	0
Fever	20 (8)	0	0	18 (7)	2 (<1)	1 (<1)
Diarrhea	18 (7)	3 (1)	0	20 (8)	2 (<1)	0
Erythema	18 (7)	2 (<1)	0	3 (1)	0	0
Weakness	14 (6)	1 (<1)	0	20 (8)	4 (2)	0
Mouth ulceration	13 (5)	1 (<1)	0	9 (4)	0	0
Hematological						
Anemia	12 (5)	2 (<1)	1 (<1)	19 (7)	3 (1)	1 (<1)
Leukopenia	5 (2)	2 (<1)	1 (<1)	27 (11)	13 (5)	9 (4)
Neutropenia	10 (4)	3 (1)	1 (<1)	25 (10)	10 (4)	9 (4)
Thrombocytopenia	3 (1)	0	0	3 (1)	0	1 (<1)

Cardiac toxicity during treatment and follow-up[1]

Table 3. Cardiotoxicity during treatment and follow-up

	No. of patients[a]	
	PLD[b] (n = 254)	Doxorubicin[c] (n = 255)
Patients who developed cardiotoxicity (LVEF defined)	10	48
Cardiotoxicity (with signs and symptoms of CHF)	0	10
Cardiotoxicity (no signs and symptoms of CHF)	10	38
Patients with signs and symptoms of CHF only	2	2

Cardiac toxicity related to cumulative dose of anthracycline[1]

Table 5. Change from baseline in LVEF by cumulative anthracycline dose[a]

Cumulative anthracycline dose		*n*	Median, %[a]	Mean, %[b]
<300 mg/m^2	PLD	62	–2.5	–2.0
	Doxorubicin	58	–6.5	–8.7
≥300 to <450 mg/m^2	PLD	54	–2.5	–2.8
	Doxorubicin	74	–7.5	–9.6
≥450 mg/m^2	PLD	36	–5.0	–2.0
	Doxorubicin	55	–16.0	–17.2
All dose ranges	PLD	152	–3.0	–2.3
	Doxorubicin	187	–8.0	–11.6

[a]Reflects cumulative dose at which the MUGA scan was performed.
[b]A negative change denotes a decrease in LVEF.
LVEF, left ventricular ejection fraction; MUGA, multigated blood-pool imaging; PLD, pegylated liposomal doxorubicin HCl (CAELYX™).

References

1 O'Brien, M. E., N. Wigler, M. Inbar, et al. 2004. "Reduced cardiotoxicity and comparable efficacy in a phase III trial of pegylated liposomal doxorubicin HCl (CAELYX/Doxil) versus conventional doxorubicin for first-line treatment of metastatic breast cancer." Ann.Oncol. 15(3):440-449.

2 Rivera, E., V. Valero, F. J. Esteva, et al. 2002. "Lack of activity of stealth liposomal doxorubicin in the treatment of patients with anthracycline-resistant breast cancer." Cancer Chemother.Pharmacol. 49(4):299-302.

3 Keller, A. M., R. G. Mennel, V. A. Georgoulias, et al. 2004. "Randomized phase III trial of pegylated liposomal doxorubicin versus vinorelbine or mitomycin C plus vinblastine in women with taxane-refractory advanced breast cancer." J.Clin Oncol. 22(19):3893-3901.

History

Version 4

Date	Summary of changes
22/10/2009	Reviewed, new dose modifications and transferred to eviQ.
14/05/2010	Cautions/Exclusions updated to Caution with prior anthracycline therapy.
28/06/2010	Haematological dose modifications updated (20% changed to 25% dose reduction).
01/07/2010	ERRATUM: in the administration details section, it should read "Administer Liposomal DOXOrubicin by IV infusion at a rate of 1 mg/min for the initial infusion".
31/08/2010	Cardiac monitoring updated to cumulative dose exceeding 600 mg/m^2 of liposomal doxorubicin.
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.

Date	Summary of changes
11/02/2011	Administration details - Pre treatment medications, dexamethasone removed and administer antiemetics if required, added.
27/04/2012	Protocol reviewed at Medical Oncology Reference Committee meeting. Next review in 2 years.
05/10/2012	Number of cycles - now includes "until maximum improvement" as per RCM April 2012.
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.
31/05/2017	Transferred to new eviQ website. Protocol version number changed to V.3. 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.4.
23/09/2019	Protocol reviewed at Medical Oncology Reference Committee meeting on 30/08/2019. No changes. Next review in 5 years.
28/07/2021	Treatment name in both protocol and patient information titles updated to doxorubicin pegylated liposomal.

First approved: 20 February 2006
Last reviewed: 30 August 2019
Review due: 31 December 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/35
08 Jun 2023

Patient information - Breast cancer metastatic - Doxorubicin pegylated liposomal

Patient's name:

Your treatment

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

Pegylated liposomal doxorubicin			
This treatment cycle is repeated every 28 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	**Liposomal Doxorubicin** (*lye-po-SO-mal dox-oh-roo-bi-sin*)	By a drip into a vein	About 1.5 to 2 hours

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.

IMMEDIATELY go to your nearest hospital Emergency Department, or contact your doctor or nurse if you have any of the following at any time:	**Emergency contact details** Ask your doctor or nurse from your treating team who to contact if you have a problem
• a temperature of 38°C or higher • chills, sweats, shivers or shakes • shortness of breath • uncontrolled vomiting or diarrhoea • pain, tingling or discomfort in your chest or arms • you become unwell.	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)	

Allergic reaction	• Allergic reactions are uncommon but can be life threatening.
	• **If you feel unwell during the infusion or shortly after it, or:**
	  ◦ **get a fever, shivers or shakes**
	  ◦ **feel dizzy, faint, confused or anxious**
	  ◦ **start wheezing or have difficulty breathing**
	  ◦ **have a rash, itch or redness of the face**
	
	<u>While you are in hospital:</u> Tell your doctor or nurse immediately.
	<u>After you leave:</u> Contact your doctor or nurse immediately, or go to the nearest hospital Emergency Department.

Nausea and vomiting	• You may feel sick (nausea) or be sick (vomit). • Drink plenty of fluids (unless you are fluid restricted). • Eat small meals more frequently. • Try food that does not require much preparation. • Try bland foods like dry biscuits or toast. • Gentle exercise may help with nausea. • Anti-sickness medication is usually not needed but may help in some people. • Ask your doctor or nurse for eviQ patient information - Nausea and vomiting during cancer treatment. • **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.**
Urine turning orange or red	• Your urine will turn an orange or red colour. • This is not harmful and should only last for up to 48 hours after treatment.
Taste and smell changes	• You may find that food loses its taste or tastes different. • These changes are likely to go away with time. • Do your mouth care regularly. • Chew on sugar-free gum or eat sugar-free mints. • Add flavour to your food with sauces and herbs. • Ask your doctor or nurse for eviQ patient information - Taste and smell changes during cancer treatment.

Early (onset days to weeks)	
Infection risk (neutropenia)	• 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. • Wash your hands often. • Keep a thermometer at home and take your temperature regularly, and if you feel unwell. • Do your mouth care regularly. • Inspect your central line site (if you have one) daily for any redness, pus or swelling. • Limit contact with people who are sick. • Learn how to recognise the signs of infection. • Ask your doctor or nurse for eviQ patient information - Infection during cancer treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms:** ◦ **a temperature of 38°C or higher** ◦ **chills, shivers, sweats or shakes** ◦ **a sore throat or cough** ◦ **uncontrolled diarrhoea** ◦ **shortness of breath** ◦ **a fast heartbeat** ◦ **become unwell even without a temperature.**
Mouth pain and soreness (mucositis)	• You may have: ◦ bleeding gums ◦ mouth ulcers ◦ a white coating on your tongue ◦ pain in the mouth or throat ◦ difficulty eating or swallowing. • Avoid spicy, acidic or crunchy foods and very hot or cold food and drinks. • Try bland and soft foods. • Brush your teeth gently with a soft toothbrush after each meal and at bedtime. If you normally floss continue to do so. • Rinse your mouth after you eat and brush your teeth, using either: ◦ 1/4 teaspoon of salt in 1 cup of warm water, or ◦ 1/4 teaspoon of bicarbonate of soda in 1 cup of warm water • Ask your doctor or nurse for eviQ patient information - Mouth problems during cancer treatment. • **Tell your doctor or nurse if you get any of the symptoms listed above.**
Tiredness and lack of energy (fatigue)	• You may feel very tired, have no energy, sleep a lot, and not be able to do normal activities or things you enjoy. • Do not drive or operate machinery if you are feeling tired. • Nap for short periods (only 1 hour at a time) • Prioritise your tasks to ensure the best use of your energy. • Eat a well balanced diet and drink plenty of fluids (unless you are fluid restricted). • Try some gentle exercise daily. • Allow your friends and family to help. • **Tell your doctor or nurse if you get any of the symptoms listed above.**

Diarrhoea	• You may get bowel motions (stools, poo) that are more frequent or more liquid. • You may also get bloating, cramping or pain. • Take your antidiarrhoeal medication as directed by your doctor. • Drink plenty of fluids (unless you are fluid restricted). • Eat and drink small amounts more often. • Avoid spicy foods, dairy products, high fibre foods, and coffee. • Ask your doctor or nurse for eviQ patient information - Diarrhoea during cancer treatment. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if your diarrhoea is not controlled, you have 4 or more loose bowel motions per day, and if you feel dizzy or light-headed.**
Appetite loss (anorexia)	• You may not feel like eating. • Try to avoid drinking fluids at meal times. • Try to eat small meals or snacks regularly throughout the day. • Try to eat food that is high in protein and calories. • If you are worried about how much food you can eat, or if you are losing weight, ask to speak to a dietitian.
Hand-foot syndrome (palmar-plantar erythrodysaesthesia)	• The palms of your hands and soles of your feet may become: ◦ red and hot ◦ swollen ◦ painful and tender ◦ blistered. • The skin in the area may also peel. • Moisturise your hands and feet daily with sorbolene or aqueous cream. • Keep your hands and feet clean and dry. • Avoid hot water, instead use lukewarm water to bathe. • Avoid direct sunlight. • Avoid unnecessary walking, jogging or exercise. • Wear cotton socks and avoid tight-fitting shoes. • **Tell your doctor or nurse as soon as possible if you notice any skin changes on your hands or feet.**
Skin reaction in an area previously treated with radiation therapy (radiation recall)	• In the area that was treated with radiation therapy, your skin may become: ◦ dry, red and itchy ◦ tender and swollen • It may also: ◦ peel or blister ◦ form ulcers • This usually happens weeks or months after chemotherapy treatment. • Avoid wearing tight clothing. • Avoid direct sunlight and very hot or cold temperatures. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and a sunscreen of SPF 50 or higher. • Tell your doctor or nurse if you get any of the symptoms listed above.

Late (onset weeks to months)	
Low red blood cells (anaemia)	• You may feel dizzy, light-headed, tired and appear more pale than usual. • Tell your doctor or nurse if you have any of these signs or symptoms. You might need a blood transfusion. • **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.**
Hair thinning	• Your hair may become dry and may break easily. • You may lose some of your hair. • Use a gentle shampoo and a soft hairbrush. • Take care with hair products like hairspray, hair dye, bleaches and perms. • Protect your scalp from the cold with a hat or scarf. • Protect your scalp from the sun with a hat and sunscreen of SPF 50 or higher. • Ask your doctor or nurse about the Look Good Feel Better program (www.lgfb.org.au)
Chemo brain (chemotherapy-related cognitive impairment)	• You may notice that you are unable to concentrate, feel unusually disorganised or tired (lethargic) and have trouble with your memory. • These symptoms usually improve once treatment is completed. • Ask your doctor or nurse for eviQ patient information – Memory changes and chemotherapy (chemo brain). • Tell your doctor or nurse if you get any of the symptoms listed above.

Delayed (onset months to years)	

Menopausal symptoms	• You may get:
	  ◦ hot flushes or night sweats
	  ◦ mood changes
	  ◦ vaginal dryness
	  ◦ irregular or no periods.
	• You may also:
	  ◦ have trouble sleeping
	  ◦ find sex painful or lose interest in sex
	• These symptoms may go away after treatment, or the menopause may be permanent.
	• If you have sex you should use contraception as there is still a risk of pregnancy. Talk to your doctor about what form of contraception is right for you.
	• Talk to your doctor or nurse about ways to manage these symptoms.

Heart problems	• You may get:
	  ◦ chest pain or tightness
	  ◦ shortness of breath
	  ◦ swelling of your ankles
	  ◦ an abnormal heartbeat.
	• Heart problems can occur months to years after treatment.
	• 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.**

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.

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.

Breast cancer information

- Australasian Lymphology Association – lymphoedema.org.au
- Australasian Menopause Society – menopause.org.au
- Breast Cancer Network Australia – bcna.org.au
- National Breast Cancer Foundation – nbcf.org.au
- YWCA Encore breast cancer exercise program – ywcaencore.org.au

General cancer information and support

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

Quit smoking information and support

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

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

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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/35
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