Multiple myeloma DT-PACE (dexamethasone thalidomide ciSplatin DOXOrubicin CYCLOPHOSPHamide etoposide)

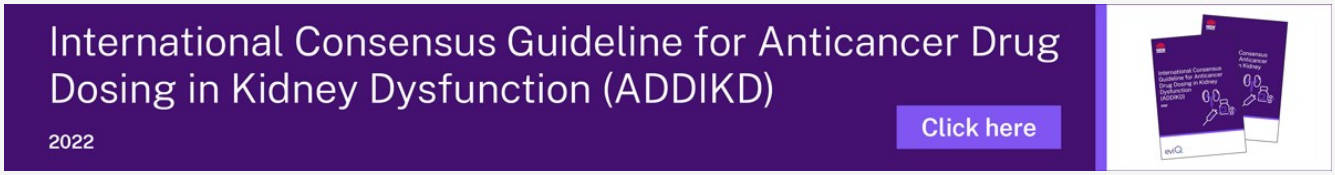
ID: 64 v.5 **Endorsed** Essential Medicine List

Patients with myeloma should be considered for inclusion into clinical trials. Link to ALLG website and ANZCTR website.

This protocol is based on limited evidence; refer to the evidence section of this protocol for more information.

Link to Medical Scientific Advisory Group (MSAG) Clinical Practice Guideline Multiple Myeloma

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 2

Drug	Dose	Route	Day
Dexamethasone	40 mg ONCE a day	PO	1 to 4
ciSplatin	10 mg/m^2	CIV over 24 hours (loaded with etoposide)	1 to 4
Etoposide	40 mg/m^2	CIV over 24 hours (loaded with cISplatin)	1 to 4
CYCLOPHOSPHamide	400 mg/m^2	CIV over 24 hours (loaded with DOXOrubicin)	1 to 4
DOXOrubicin	10 mg/m^2	CIV over 24 hours (loaded with CYCLOPHOSPHamide)	1 to 4
Thalidomide *	400 mg ONCE a day	PO	1 to 28

***** Consider a starting dose of thalidomide 100 mg daily and increase as tolerated. Thalidomide may be dose reduced or omitted.

Note: the schedule presented differs from the administration as per original study by Lee et al.,[1] in which the daily dose of cisplatin, cyclophosphamide, and etoposide was combined in a 1-L bag of 0.9% normal saline, and doxorubicin was infused separately in more than 50 mL of 5% dextrose in water each day. Other trials used different dosing and schedules, please refer to the reference section .

Frequency: 28 days

Cycles: 2 to 4

Notes:

- The optimal dose of thalidomide varies according to the individual patient and opinions on dosing vary among clinicians and institutions. Individuals with myeloma are often started at 50 to 100 mg per day, and the dose increased every 1 to 2 weeks as tolerated.

- Administer with caution within 4 weeks of radiation therapy.
- The use of G-CSF is frequently required to maintain the schedule.
- This protocol may be used for mobilisation of peripheral blood haematopoietic stem cells. The dose of filgrastim for mobilisation is 10 micrograms/kg/day and should be commenced from day +5.

Drug status: **Thalidomide:** (**PBS authority**)

NB: patient registration into a pregnancy prevention risk management program is required.

All other drugs in this protocol are on the PBS general schedule

Thalidomide is available as **50 mg** and **100 mg** capsules
Dexamethasone is available as **4 mg** and **0.5 mg** tablets

Cost: ~ $2,590 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 2

Day 1 to 4		
Dexamethasone	40 mg (PO)	ONCE a day on days 1 to 4. Take in the morning with food.
ciSplatin	10 mg/m^2 (CIV over 24 hours)	in 1000 mL sodium chloride 0.9% loaded with etoposide as a continuous infusion for 24 hours
Etoposide	40 mg/m^2 (CIV over 24 hours)	in 1000 mL sodium chloride 0.9% loaded with cISplatin as a continuous infusion for 24 hours
CYCLOPHOSPHamide	400 mg/m^2 (CIV over 24 hours)	in 1000 mL sodium chloride 0.9% loaded with DOXOrubicin as a continuous infusion for 24 hours
DOXOrubicin	10 mg/m^2 (CIV over 24 hours)	in 1000 mL sodium chloride 0.9% loaded with CYCLOPHOSPHamide as a continuous infusion for 24 hours
Thalidomide	400 mg (PO)	ONCE a day.Take in the evening at least one hour after food.*

Day 5 to 28		
Thalidomide	400 mg (PO)	ONCE a day.Take in the evening at least one hour after food.*

***** Consider a starting dose of thalidomide 100 mg daily and increase as tolerated. Thalidomide may be dose reduced or omitted.

Note: the schedule presented differs from the administration as per original study by Lee et al.,[1] in which the daily dose of cisplatin, cyclophosphamide, and etoposide was combined in a 1-L bag of 0.9% normal saline, and doxorubicin was infused separately in more than 50 mL of 5% dextrose in water each day. Other trials used different dosing and schedules, please refer to the reference section .

- The use of G-CSF is frequently required to maintain the schedule.
- This protocol may be used for mobilisation of peripheral blood haematopoietic stem cells. The dose of filgrastim for mobilisation is 10 micrograms/kg/day and should be commenced from day +5.

Frequency: 28 days

Cycles: 2 to 4

Indications and patient population

- Relapsed/refractory multiple myeloma

Clinical information

Caution with oral anti-cancer drugs	Select links for information on the safe prescribing, dispensing and administration of orally administered anti-cancer drugs. Read more about the COSA guidelines and oral anti-cancer therapy
Venous access	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 etoposide.
Antiemetics for multi-day protocols	Antiemetic therapy should be administered throughout the duration of the chemotherapy protocol and to cover delayed nausea. The acute and delayed emetic risk of multi-day chemotherapy protocols will overlap depending on the individual drugs and their sequence of administration. More or less antiemetic cover may be required. As a steroid has been included as part of this protocol, additional antiemetic steroids are not required. 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

Teratogenic effects	Immunomodulatory drugs (IMiDs) include thalidomide, lenalidomide and pomalidomide. They can cause severe congenital disabilities or death to an unborn baby when taken during pregnancy. All patients and partners of patients that can conceive a child must use at least one reliable contraceptive method for at least 4 weeks before starting treatment, during treatment (including dose interruptions), and for 4 weeks after stopping treatment. Male patients should also use a condom when having sexual intercourse with a woman of childbearing potential during treatment (including dose interruptions), and for 4 weeks after stopping treatment. In female patients and female partners of male patients, a pregnancy test should be carried out prior to initiating treatment (after 4 weeks of contraception use), weekly during the first month of treatment and monthly thereafter. Effective contraception methods and adequate contraception timeframes should be discussed with all patients of reproductive potential. Prescription of an IMiD requires patient registration with a pregnancy prevention program. Full prescribing information and Authority Application forms available from the Department of Human Services website
Etoposide conversion factor	Note: Etopophos (etoposide phosphate) 113.6 mg is equivalent to etoposide 100 mg. Doses in this protocol are expressed as etoposide.
Compatibility of drugs for DT-PACE protocol	The compatibility of combinations of doxorubicin, cyclophosphamide, cisplatin and etoposide used in the DT-PACE can be found in the compatibility of drugs for the DT-PACE protocol document.
Thromboembolism	Patients are at an increased risk of venous thrombosis with this treatment. Risk assessment for VTE should be performed prior to and during treatment. It is the consensus opinion of the Haematology Reference Committee that concomitant thromboprophylaxis is recommended: consider using low dose aspirin for patients without pre-existing risk factors, while patients with pre-existing risk factors should receive enoxaparin 40 mg subcut daily for the duration of treatment (unless contraindicated; reduce dose in renal impairment) Read more about the prophylaxis of venous thromboembolism (VTE) in multiple myeloma
Thalidomide induced constipation	Prescribe prophylactic laxatives to prevent thalidomide-induced constipation.
Peripheral neuropathy	Baseline neurotoxicity assessment recommended. Monitor for sensory changes. Dose modifications may be required. **Caution**: Thalidomide-induced peripheral neuropathy may be permanent and may impact on future treatment choices Read more about peripheral neuropathy Link to chemotherapy-induced peripheral neuropathy screening tool
Bone modifying agents	Use of a bone modifying agent (BMA) should be considered in all patients with symptomatic myeloma requiring treatment. For patients with newly diagnosed symptomatic myeloma, zoledronic acid, pamidronate or denosumab should be considered for monthly administration (adjust for kidney dysfunction where appropriate) for up to 2 years. A longer duration of therapy may be appropriate (MRC M IX trial).[2] For more information, please see the following protocols: ID 137 Multiple myeloma zoledronic acid ID 147 Multiple myeloma pamidronate ID 3964 Multiple myeloma denosumab - note denosumab is TGA approved but not PBS reimbursed for this indication.
Bisphosphonates and dental review	Caution should be taken with prolonged use of bisphosphonates due to the risk of osteonecrosis of the jaw (ONJ). A dental review prior to treatment is recommended, and all dental issues treated before the initiation of bisphosphonates. Dental review 6 to 12 monthly during treatment is advisable to minimise risk of ONJ. Concurrent daily oral supplements of calcium 500 mg and vitamin D 400 International Units are recommended. Read more about medication-related osteonecrosis of the jaw (MRONJ)

Corticosteroids	Diabetic patients should monitor their blood glucose levels closely. To minimise gastric irritation, advise patient to take immediately after food. Consider the use of a H2 antagonist or proton pump inhibitor if appropriate. Read more about acute short term effects from corticosteroids
Tumour lysis risk	Assess patient for risk of developing tumour lysis syndrome. Read more about prevention and management of tumour lysis syndrome.
Pneumocystis jirovecii pneumonia (PJP) prophylaxis	Read more about prophylaxis of pneumocystis jiroveci (carinii) in cancer patients
Antifungals and antivirals	There are no specific recommendations for the use of antifungal or antiviral prophylaxis with this treatment. The use of prophylaxis should be at the discretion of the treating clinician and based on patient risk factors and local guidelines. Read more about antifungal and antiviral prophylaxis
Growth factor support	G-CSF (short or long-acting) is available on the PBS for chemotherapy induced neutropenia depending on clinical indication and/or febrile neutropenia risk. Access the PBS website
Blood tests	FBC, EUC and LFTs at baseline and prior to each treatment or as clinically indicated
Hepatitis B screening and prophylaxis	Routine screening for HBsAg and anti-HBc is recommended prior to initiation of treatment. Prophylaxis should be determined according to individual institutional policy. 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 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. 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
Delay treatment until absolute neutrophil count (ANC) greater than 1.0 x 10^9/L and platelets greater than 100 x 10^9/L

Renal impairment	
eGFR (CKI-EPI or MDRD) or eCrCl (Cockcroft Gault) (mL/min)*	
greater than or equal to 70	No dose modifications necessary
50 to less than 70	Reduce cisplatin by 25%
30 to less than 50	Reduce etoposide by 25% and cisplatin by 50% or consider substituting cisplatin with carboplatin
10 to less than 30	Reduce etoposide by 50% and omit cisplatin or consider substituting cisplatin with carboplatin
less than 10	Reduce etoposide by 50% and cyclophosphamide by 25% and omit cisplatin or consider substituting cisplatin with carboplatin

** Each method has its limitations. Refer to Nephrotoxicity associated with cisplatin for more information.*

Note: *Omit cisplatin in dialysis dependent patients.*

Hepatic impairment	
Bilirubin (micromol/L)	
25 to 50	Reduce doxorubicin and etoposide by 50%
51 to 85	Reduce doxorubicin and etoposide by 75%
greater than 85	Omit doxorubicin and etoposide

Peripheral sensory neuropathy	
Grade 2	Withhold thalidomide until peripheral neuropathy resolves to Grade 1, then reinstate at 50% dose reduction. If sensory neuropathy is associated with neuropathic pain, cease thalidomide.[3]
Grade 3	Cease thalidomide

Caution: *Thalidomide-induced peripheral neuropathy may be permanent and may impact on future treatment choices.*

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*

Cisplatin		
	Interaction	**Clinical management**
Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, cisplatin, contrast dye, frusemide, NSAIDs)	Additive nephrotoxicity	Avoid combination or monitor renal function closely
Ototoxic drugs (e.g. aminoglycosides, frusemide, NSAIDs)	Additive ototoxicity	Avoid combination or perform regular audiometric testing
Neurotoxic drugs (e.g. vincristine, paclitaxel)	Additive neurotoxicity	Monitor closely for neuropathy if combination used
Paclitaxel	Administration schedule may influence the development of myelosuppression	Minimise toxicity by administering paclitaxel first in regimens using the combination
Carbamazepine, phenytoin, valproate	Decreased antiepileptic plasma levels	Monitor antiepileptic serum levels and seizure frequency for efficacy; adjust dosage as appropriate or select alternative antiepileptic (e.g. clonazepam, diazepam, lorazepam)

Cyclophosphamide		
	Interaction	**Clinical management**
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Increased toxicity of cyclophosphamide possible due to increased conversion to active (and inactive) metabolites	Avoid combination or monitor for cyclophosphamide toxicity
CYP3A4 inhibitors (e.g. aprepitant, azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)	Reduced efficacy of cyclophosphamide possible due to decreased conversion to active (and inactive) metabolites	Avoid combination or monitor for decreased clinical response to cyclophosphamide
Amiodarone	Possible additive pulmonary toxicity with high-dose cyclophosphamide (i.e. doses used prior to stem cell transplant; 60 mg/kg daily or 120 to 270 mg/kg over a few days)	Avoid combination or monitor closely for pulmonary toxicity
Allopurinol, hydrochlorothiazide, indapamide	Delayed effect. Increased risk of bone marrow depression; probably due to reduced clearance of active metabolites of cyclophosphamide	Avoid combination, consider alternative antihypertensive therapy or monitor for myelosuppression
Ciclosporin	Reduced efficacy of ciclosporin due to reduced serum concentration	Monitor ciclosporin levels; adjust dosage as appropriate; monitor response to ciclosporin
Suxamethonium	Prolonged apnoea due to marked and persistent inhibition of cholinesterase by cyclophosphamide	Alert the anaesthetist if a patient has been treated with cyclophosphamide within ten days of planned general anaesthesia

Dexamethasone		
	Interaction	**Clinical management**
CYP3A4 interactions	Dexamethasone is a substrate of CYP3A4 and a weak to moderate inducer of CYP3A4. The clinical relevance of CYP3A4 induction by dexamethasone is unknown as the mechanism has yet to be established	The effects of the concomitant use of dexamethasone with other CYP3A4 inducers, inhibitors or substrates is variable. If used concomitantly, monitor patients closely for adverse drug reactions
Warfarin	Concurrent use may result in increased risk of bleeding or diminished effects of warfarin	Monitor prothrombin time / INR (especially during initiation or discontinuation) and for signs of drug toxicity during concomitant use; adjust warfarin dose as required
Oral hypoglycaemics	Corticosteroids may cause hyperglycaemia and worsen diabetes control	Monitor blood glucose levels and adjust oral hypoglycaemic dose as required

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

Etoposide and Etoposide Phosphate		
	Interaction	**Clinical management**
CYP3A4 and P-gp inhibitors (e.g. amiodarone, aprepitant, azole-antifungals, ritonavir, lapatinib, nilotinib, sorafenib, macrolides, ciclosporin etc.)	Increased toxicity of etoposide possible due to reduced clearance	Avoid combination or monitor for etoposide toxicity
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of etoposide possible due to increased clearance	Avoid combination or monitor for decreased clinical response to etoposide
Glucosamine	Reduced efficacy of etoposide (due to induction of glucose-regulated stress proteins resulting in decreased expression of topoisomerase II)	Avoid combination or monitor for decreased clinical response to etoposide
Grapefruit juice	Reduced efficacy of oral etoposide possible due to possible alteration of P-gp mediated intestinal transport of etoposide	Avoid combination or monitor for decreased clinical response to etoposide

Thalidomide		
	Interaction	**Clinical management**
Zoledronic acid	Increased risk of renal dysfunction	Monitor renal function
Hormonal therapy (combined oral contraceptive, HRT), erythropoietic agents, corticosteroids	Additive risk of thromboembolic events	Alternative methods of contraception must be used in women of childbearing potential; thromboprophylaxis should be considered according to risk assessment
Drugs associated with peripheral neuropathy (e.g. amiodarone, antiretrovirals, bortezomib, isoniazid, nitrofurantoin, vincristine etc.)	Increased risk of peripheral neuropathy	Avoid combination or monitor closely for peripheral neuropathy
CNS depressants (including opiates, opioids, phenothiazines)	Additive CNS depressant effects (e.g. drowsiness, ataxia)	Avoid combination or monitor for excessive CNS depression
Drugs associated with bradycardia, orthostatic hypotension (e.g. beta blockers, diuretics, donepezil etc.)	Additive bradycardic, hypotensive effect	Caution advised if combination used - monitor heart rate and counsel patient on falls prevention

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.

Days 1 to 4

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

Peripheral neuropathy assessment tool

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

- baseline weight

Note: A large volume of intravenous fluid may be given with this protocol. If weight increases by more than 1 kg from baseline or fluid balance becomes positive by one litre or any other signs of fluid overload are present, review by medical officer (diuretics may be required).

Prime IV line(s).

Access CVAD.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Dexamethasone

- administer orally ONCE a day in the morning
- to be taken with or immediately after food.

Note: if a dose is forgotten or vomited, contact treating team.

Chemotherapy - Time out

Commence prehydration for cisplatin

- Administer 10 mmol magnesium sulphate ($MgSO_4$) in 1000 mL sodium chloride 0.9% over 60 minutes.
- Ensure patient has passed urine prior to cisplatin administration as per institutional policy.

Note:

- Mannitol 10% may be used as per institutional policy; there is much variation in the use of mannitol and although there is no conclusive evidence that mannitol should be used, many sites have used it routinely without renal toxicity. The routine use of frusemide to increase urine flow is not recommended. Refer to your institutional guidelines and medical orders. For more information, see prevention and management of cisplatin nephrotoxicity.

Note: Bag 1 and bag 2 are to run concurrently.

Etoposide and cisplatin infusion

Administer etoposide and cisplatin (irritant) :

- via IV infusion over 24 hours
- via second line attached to a separate lumen of the CVC
- commence bag 1 containing the etoposide and cisplatin
- these drug are mixed together (by the pharmacy department) in the same bag and administered concurrently with bag 2
- check the amount in the bag is the amount prescribed for a 24 hour period only
- observe for hypersensitivity
  - if severe hypersensitivity reaction occurs do not rechallenge
- flush with ~ 100 mL sodium chloride 0.9%
- at the end of each 24 hour period, use new IV giving sets for next doses of chemotherapy.

Doxorubicin and cyclophosphamide

Administer doxorubicin and cyclophosphamide (vesicant):

- via IV infusion over 24 hours
- via one line attached to one lumen of the CVC
- commence bag 2 containing the doxorubicin and cyclophosphamide
- these drug are mixed together (by the pharmacy department) in the same bag and administered concurrently with bag 1
- check the amount in the bag is the amount prescribed for a 24 hour period only
- at the end of each 24 hour period, use new IV giving sets for next doses of chemotherapy.

Hydration if prescribed

Treatment - Time out

Thalidomide

- administer orally ONCE a day in the evening on **days 1 to 28**
- to be swallowed whole with a glass of water; do not break, crush or chew
- to be taken at least one hour after food

Note: missed doses should not be taken if it is less than 12 hours until the next dose.

Deaccess CVAD.

Continue safe handling precautions until 7 days after completion of drug(s)

Days 5 to 28

This is an oral treatment

Safe handling and waste management (reproductive risk only)

Safe administration

General patient assessment prior to each day of treatment.

Peripheral neuropathy assessment tool

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

Treatment - Time out

Thalidomide

- administer orally ONCE a day in the evening on **days 1 to 28**
- to be swallowed whole with a glass of water; do not break, crush or chew
- to be taken at least one hour after food

Note: missed doses should not be taken if it is less than 12 hours until the next dose.

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

Discharge information

Antiemetics

- Antiemetics as prescribed.

Thalidomide capsules

- Thalidomide capsules with written instructions on how to take them.

Thromboprophylaxis

- Low dose aspirin OR enoxaparin 40 mg subcut daily for the duration of treatment if prescribed.

Laxatives

- Ensure patient has prophylactic laxatives.

Growth factor support

- Arrangements for administration if prescribed.

Prophylaxis medications

- Prophylaxis medications (if prescribed) i.e. tumour lysis prophylaxis, PJP prophylaxis, antivirals.

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)	
Extravasation, tissue or vein injury	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 extravasation management

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
Thrombocytopenia	A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding. Read more about thrombocytopenia
Constipation	
Dizziness and orthostatic hypotension	The feeling of being lightheaded, weak or unsteady, which may lead to fainting. Orthostatic hypotension may cause dizziness. Patients should be advised to stand up slowly from a sitting or lying position and to increase fluid intake if feeling dehydrated.
Drowsiness and sedation	Drowsiness (the feeling of being abnormally sleepy or tired during the day) and sedation (the reduction of irritability or agitation to produce a state of calm or sleep) commonly occurs with thalidomide but is usually mild and dose dependent.
Fatigue	Read more about fatigue
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting
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
Peripheral neuropathy	Typically symmetrical sensory neuropathy, affecting the fingers and toes, sometimes progressing to the hands and feet. It is associated with several classes of anti-cancer drugs. These include taxanes, platinum-based compounds, vinca alkaloids and some drugs used to treat multiple myeloma. Read more about peripheral neuropathy
Side effects of corticosteroids	Insomnia, oedema, increased risk of infection e.g. oral thrush, gastric irritation, worsening of peptic ulcer disease, increased blood sugar levels, loss of diabetic control, mood and behavioural changes - including anxiety, euphoria, depression, mood swings, increased appetite and weight gain, osteoporosis and fractures (long term use), bruising and skin fragility are associated with corticosteroid use.
Skin rash	Anti-cancer drugs can cause a number of changes in the skin with maculo-papular rash the most common type of drug-induced skin reaction. Read more about skin rash
Thromboembolism	Venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE) is significantly increased in multiple myeloma patients treated with thalidomide in combination with other therapies including doxorubicin, melphalan and prednisolone or dexamethasone; and lenalidomide and pomalidomide in combination with dexamethasone. Read more about management of thromboembolism (VTE) in multiple myeloma

Late (onset weeks to months)	
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia
Alopecia	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 alopecia and scalp cooling

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
Pulmonary toxicity	Pulmonary toxicity may include damage to the lungs, airways, pleura and pulmonary circulation. Read more about pulmonary toxicity associated with anti-cancer drugs

Evidence

DT-PACE is an intensive, multi-chemotherapy regimen and has been prospectively studied in the "pre-novel agent" era by Lee et al,[1] and more recently retrospectively assessed in series of patients including a significant proportion who had received prior immunomodulatory drug (IMID) or proteasome inhibitor based therapy.[4]

Lee et al prospectively enrolled 236 patients in a study to evaluate the comparative efficacy of DT-PACE when compared to tandem autologous transplantation in previously treated patients with myeloma. Patients were aged between 31 and 84 years. Of the 236 enrolled patients, 7 never started treatment, 6 patients were dialysis-dependent and had cisplatin withheld and another 67 patients had < 50% dose treatment either because of age or co-morbidity. Before being treated with DT-PACE, 148 patients (63%) had shown progressive disease while receiving standard chemotherapy, and 55 patients (23%) had chromosome 13 abnormalities.[1]

Gerrie et al retrospectively analysed the outcomes of 75 patients with relapsed or refractory myeloma treated between 1999 to 2010 at either PMH Toronto or the Mayo clinic Scottsdale. Patients had a median age of 56 and had received a median of 3 prior treatment regimens. 49% had received prior thalidomide, 23% had lenalidomide, 32% had bortezomib. 33% had received a prior autologous stem cell transplant (ASCT)(the non-transplanted patients wither had had rapidly progressive disease, poor performance status or other organ impairment precluding transplant or were too old). 20% of patients had secondary plasma cell leukaemia, and 4% leptomeningeal disease.[4]

Both the prospective study by Lee et al[1] and the retrospective analysis of salvage DT-PACE by Gerrie et al[4] confirm that it is an efficacious choice as a salvage regimen in relapsed/refractory myeloma (even with prior exposure to novel agents or prior ASCT), particularly as a bridge to transplantation. It is important to note however there are several differences between these studies in terms of the protocol delivered, as well as toxicity outcomes. In the Gerrie retrospective, thalidomide was omitted entirely in many of the cycles administered (62%) i.e. DPACE was given rather than DT-PACE.

Also, the median dose of thalidomide achieved (200 mg) was much lower than in the Lee study (target 400 mg) suggesting that to obtain a response with this regimen, full dose thalidomide is less important than delivering the 'traditional' cytotoxics. The lower rates of thromboembolism, constipation and neuropathy seen in this retrospective study probably reflect the lower dose or omission of thalidomide. Electrolyte disturbances were seen more frequently in the retrospective analysis and close monitoring is recommended and routine electrolyte supplementation may be of benefit.[1]

Source	Study & Year Published	Supports Use	Is the dose and regimen consistent with the protocol?	Comments
Phase II trials	Lee et al. 2003[1]	**Yes**	Yes	-
Case series	N/A	**N/A**	N/A	-
Observational studies	Gerrie et al. 2013[4]	**Yes**	No	The median dose of thalidomide was 200 mg
Guidelines	**Date published/revised**	**Supports Use**	**Is the dose and regimen consistent with the protocol?**	**Comments**
MSAG	V.4.2017	**Yes**	Yes	Number of cycles recommended is 3 - 6
NCCN	V.1.2020	**Yes**	No	Thalidomide dose range was 50 - 200 mg
BCCA	N/A	**N/A**	N/A	-

CCO	N/A	**N/A**	N/A	-

Efficacy

In Lee et al[1], 229 patients were evaluated for response to two cycles of DT-PACE for induction. The partial remission rate (PR) after 2 cycles of DT-PACE was 32%, with 16% attaining a complete response (CR) or near-CR (n-CR) (defined as only immunofixation electrophoresis-positive). Patients who received a 100% dose of DT-PACE for two cycles (n = 115) achieved higher response rates than those with less than 100% dose (n = 121): PR or better, 49% vs 17% ($p < 0.0001$); CR + nCR, 27% vs 6% ($p < 0.0001$).

Patients with high lactate dehydrogenase (LDH) (n = 98) showed a better response than those with a normal LDH (n = 138): PR or better 43% vs 27% ($p = 0.01$), CR + nCR, 25% vs 11% ($p = 0.01$). Patients with chromosome 13 abnormalities (n = 55) responded equally well as the other patients (n = 181): PR or better, 35% vs 33% ($p = 0.84$); CR + nCR, 17% vs 15% ($p = 0.73$).[1]

In Gerrie et al[4], of the 75 patients evaluated 90% completed a median of two cycles. 50% (n = 37) completed one cycle and 40% (n = 30) two cycles. Overall response rate (ORR) was 49% (partial response 33% and very-good partial response 16%). An additional 36% of patients had stable disease (SD) and 9% progressed on treatment. CR rates were not reported.

The median progression-free survival (PFS) was 5.5 months (95% CI 4.3-9.8) and median OS 14 months (95% CI 8.7-19.3). However, 35 of 64 patients who responded or had stable disease proceeded to ASCT or a clinical trial with median PFS for this subset of 13.4 months (CI 7.7-20.1), and median OS 20.5 months (CI 14.8-63.8).[4]

Eastern Cooperative Oncology Group status (ECOG) 3 - 4 patients had significantly poorer OS (5.5. vs 15.9) and PFS (2.6 vs 5.5 months) in comparison to ECOG status 0-2 patients. Those who had already received a prior ASCT had poorer outcomes (OS 7.5 vs no prior ASCT 15.9).[4]

A phase 2 study 'The Total Therapy 3'[5] added bortezomib (1.0 mg/m^2 on days 1,4,8 and 11) to the DT PACE backbone for 303 newly diagnosed patients with myeloma. Induction chemotherapy prior to and consolidation chemotherapy after tandem transplants each consisted of two cycles of VTD-PACE (bortezomib, thalidomide, dexamethasone and 4-day continuous infusions of cisplatin, doxorubicin, cyclophosphamide, etoposide) with the thalidomide dose capped at 200 mg daily. At 24 months, 83% had completed near-complete remission.

Toxicity

Although tolerated well overall, only approximately 50% patients were able tolerate full doses of DT-PACE. Toxicity was monitored for 3 months after the first 2 induction cycles of DTPACE. Grades ≥ 2 neutropenia occurred in 65% of patients with neutropenic fever observed in 12% and lasting a median of 5 days. Grades ≥ 2 thrombocytopenia occured less frequently at 11% and was associated with 22 haemorrhagic events - 8 episodes of gastrointestinal (GI) mucosal bleeding, 8 haematuria, 2 serious epistaxis and 5 bleeds at central venous access devide entry sites. Other toxicities are summarised below.[1]

Toxicity[1]	All grades (%)	Grade 3-4 (%)
ANC < 0.5 X 10^9/L	39	-
Platelets < 75 x 10^9/L	48	-
Neutropenic fever	12	9
Nausea and vomiting	21	6
Stomatitis	19	4
Gastritis/oesophagitis	5	2
Diarrhoea	8	2
Constipation	18	0
Congestive heart failure	1	1
Thromboembolism	15	5
Sensory neuropathy	13	4

In Gerrie et al[4], haematological toxicity was common with grade 3-4 anaemia (Hb <80 g/l) occurring in 48% and grade 3-4 thrombocytopenia (PLT <50 x 10^9/l) occurring in 69% of patients. Bleeding occurred in 17 of 75 patients however grade 3 bleeding only occurred in 2 patients (epistaxis and haematuria). Grade 3-4 neutropenia occurred in 88%, despite 76% receiving GCSF support. The median day of ANC nadir was D 11.

Febrile neutropenia occurred in 21 patients. In order to achieve the modest rates of infection/febrile neutropenia, 64% of patients

were given prophylactic antibiotics (described as “Antifungal, antiviral, antibiotics”) at clinician discretion. Treatment related death was documented in 5% of patients (neutropenic sepsis X 2, PE and a GI bleed).

Other non-haematologic toxicities included frequent electrolyte disturbances with hypocalcaemia and hypomagnesaemia recorded in 69% and 60% of patients respectively (grade 3-4 occurring in 10 and 12% respectively).

The regimen was only moderately emetogenic with nausea and vomiting of any grade occurring in 21% of cycles (2% grade 3-4) however anti-emetic prophylaxis was not documented. Other notable toxicities were mucositis in 17% (but of grade 3-4 in only 4%), new or worsening renal insufficiency in 14% of cycles and neuropathy 10% (grade 3-4 only 3%).[4]

References

1 Lee CK, Barlogie B, Munshi N et al. 2003. DTPACE: an effective, novel combination chemotherapy with thalidomide for previously treated patients with myeloma. J Clin Oncol 21(14):2732-2739

2 Morgan, G. J., J. A. Child, W. M. Gregory, et al. 2011. "Effects of zoledronic acid versus clodronic acid on skeletal morbidity in patients with newly diagnosed multiple myeloma (MRC Myeloma IX): secondary outcomes from a randomised controlled trial." Lancet Oncol 12(8):743-752.

3 Delforge, M., J. Blade, M. A. Dimopoulos, et al. 2010. "Treatment-related peripheral neuropathy in multiple myeloma: the challenge continues." Lancet Oncol 11(11):1086-1095.

4 Gerrie, A. S., J. R. Mikhael, L. Cheng, et al. 2013. "D(T)PACE as salvage therapy for aggressive or refractory multiple myeloma." Br J Haematol 161(6):802-810.

5 Barlogie, B., E. Anaissie, F. van Rhee, et al. 2007. "Incorporating bortezomib into upfront treatment for multiple myeloma: early results of total therapy 3." Br J Haematol 138(2):176-185.

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History

Version 5

Date	Summary of changes
23/08/2008	Added S100 form for download.
31/10/2008	Addition of information regarding counselling pre-thalidomide, more clear information re contraception requirements, recommended premedication, bisphosphonates and clinical considerations. More drug interactions added and patient information sheet re-written. Combination of drugs for infusion changed.
07/09/2009	Reviewed and transferred to eviQ.
15/01/2010	Update of S100 restriction for thalidomide.
30/07/2010	Update of thalidomide i-access™ program details; VTE recommendations; PCP prophylaxis recommendations; contraception recommendations and FAQs in patient information; removal of aspirin general interaction.
19/01/2012	PHC view created.
24/02/2012	New format to allow for export of protocol information. Protocol version number changed to v.2. Antiemetics and premedication 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.
31/08/2012	Protocol reviewed using the stratified review process at the Haematology Reference Committee meeting.

Date	Summary of changes
	No change and next review in 2 years.
18/06/2013	Added new bisphosphonate and VTE clinical information blocks as per Kwan's request and republished.
13/03/2015	Reviewed at Haematology Reference Committee meeting: • Evidence updated, added Scottsdale and PMH Toronto studies. • Changed the indication to relapsed/refractory patients. • Updated the emetogenicity clinical information block. • Added note that thalidomide can be dose reduced or omitted. • Adopted standard eviQ renal impairment dose modifications for cisplatin.
18/10/2015	Removed reference to 'i-Access™ Program'.
31/05/2017	Transferred to new eviQ website. Version number change to v.4.
24/11/2017	Reviewed post Haematology Reference Committee meeting: • Added note under treatment schedule. • Reference to the 'i-Access™ program' added back into drug status. • Dose modification updated as per Delforge et al 2010 paper. • Evidence updated. • Version number increased to v.5.
24/05/2019	Protocol reviewed at the Haematology Reference Committee meeting. Discussion continued over email and protocol approved with the following changes: • Note underneath the treatment schedule updated. • Blood tests updated. • Side effects updated to include nausea and vomiting as early side effects. • Limited evidence flag added in retrospect. • Evidence updated. • To be reviewed in 5 years.
10/10/2019	Clinical information updated with PBS expanded indications for GCSF.
05/05/2021	Cisplatin prehydration advice updated in administration section.
20/01/2022	Interactions updated.
24/01/2022	Pulmonary toxicity added to side effects.
14/10/2022	The following changes have been made with the consensus agreement of the Haematology Reference Committee: • Bone modifying agents block added to clinical information, related note removed from treatment schedule and linked pages removed • Link to Medical Scientific Advisory Group (MSAG) guidelines updated • Changed all references of 'i-Access™ program' to 'pregnancy prevention risk management program'

First approved: 31 August 2012
Last reviewed: 24 May 2019
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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/p/64
09 Jun 2023

Patient information - Multiple myeloma - DT-PACE (dexamethasone, thalidomide, cisplatin, doxorubicin, cyclophosphamide, etoposide)

Patient's name:

Your treatment

The treatment schedule below explains how the drugs for this treatment are given.

DT-PACE (dexamethasone, thalidomide, cisplatin, doxorubicin, cyclophosphamide, etoposide)			
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 to 4	**Dexamethasone** (*dex-a-METH-a-sone*)	Take orally ONCE a day in the morning with food on days 1 to 4 only.	
	Cisplatin *(siss-PLAT-in)*	By drip into a vein	For 4 days (96 hours) continuously
	Etoposide *(e-TOE-poe-side)*	By drip into a vein	
	Cyclophosphamide (*SYE-kloe-FOS-fa-mide*)	By drip into a vein	
	Doxorubicin (*dox-oh-roo-bi-sin*)	By drip into a vein	
1 to 28	**Thalidomide** (*tha-LID-oh-mide*)	Take orally ONCE a day in the evening on days 1 to 28 at least one hour after food. Swallow whole, do not break, open, chew or crush capsules.	

Missed doses:

- **Dexamethasone**: if you forget to take your tablets or vomit your tablets, contact your treating team.
- **Thalidomide**: if you forget to take a capsule and if it less than 12 hours before your next dose, skip that dose and take your normal dose at the next time it is due. Do not take an extra dose.

When to get help

Anticancer drugs (drugs used to treat cancer) can sometimes cause serious problems. It is important to get medical help immediately if you 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 38ºC or higher	Daytime: Night/weekend:

- chills, sweats, shivers or shakes
- shortness of breath
- uncontrolled vomiting or diarrhoea
- pain, tingling or discomfort in your chest or arms
- you become unwell.

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).

Important information about taking thalidomide

Thalidomide is only available under a restricted distribution pregnancy prevention risk management program. You, your doctor and your pharmacist must be registered and comply with conditions of the pregnancy prevention risk management program.

Thalidomide can cause major birth defects to an unborn baby. Thalidomide must not be taken if you are pregnant. Contraception **must** be used while you are being treated with thalidomide.

- **If you are a male patient and your female partner is of child-bearing potential** you **must** use condoms while taking thalidomide and for four weeks after finishing thalidomide treatment.
- **If you are a woman of child-bearing potential (a patient or a partner of a patient)** you **must** use at least one effective method of contraception during treatment with thalidomide. You should start using contraception four weeks before taking thalidomide and continue for four weeks after finishing thalidomide treatment. It is important that you discuss appropriate contraception with your doctor.

It is preferable that you use at least one additional effective method of contraception (diaphragm, cervical cap or condom by your male partner). If you are unsure please ask your doctor or nurse for advice.

If you have sexual contact without contraception even once, you must stop taking thalidomide and tell your doctor immediately. If you are a woman who is still able to have children and you miss a period during treatment, you must stop taking thalidomide and tell your doctor immediately. If you are a male patient and your female partner is able to have children and she misses a period during your treatment you must inform your doctor immediately.

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.

Central venous access devices (CVADs)

This treatment involves having chemotherapy through a central venous access device (CVAD). Your doctor or nurse will explain this to you. For more information see the eviQ patient information sheets on CVADs.

Treatment with cyclophosphamide

You should drink at least 8 to 10 glasses of fluid (unless you are fluid restricted) for 2 days after treatment with cyclophosphamide.

You should also empty your bladder often.

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.
- **Blood clot prevention medication:** you may be given low dose aspirin or daily injections of a drug called enoxaparin to prevent blood clots. Your doctor will decide if you need this medication.
- **Laxatives:** you may be given some medication to prevent or treat constipation. Your doctor or nurse will tell you how and when to take the laxatives.
- **Prophylaxis medication:** you may need to take some medications to prevent infection and to help prevent or reduce some of the side effects of the chemotherapy. Your doctor or nurse will tell you how and when to take these medications.
- **G-CSF:** you may be given injection(s) of a drug called G-CSF (also called filgrastim, lipegfilgrastim or pegfilgrastim) under your skin. This helps to boost your white blood cell count. Your white blood cells help to fight infection. Lipegfilgrastim and pegfilgrastim are given once. Filgrastim is given for several days until your white blood cells recover. Your doctor will decide if you need this medication.

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)	
Pain or swelling at injection site (extravasation)	• This treatment can cause serious injury if it leaks from the area where it is going into the vein. • This can cause pain, stinging, swelling or redness at or near the site where the drug enters the vein. • If not treated correctly, you may get blistering and ulceration. • **Tell your doctor or nurse immediately if you get any of the symptoms listed above during or after 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.**
Low platelets (thrombocytopenia)	• 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. • Try not to bruise or cut yourself. • Avoid contact sport or vigorous exercise. • Clear your nose by blowing gently. • Avoid constipation. • Brush your teeth with a soft toothbrush. • Don't take aspirin, ibuprofen or other similar anti-inflammatory medications unless your doctor tells you to. • Tell your doctor or nurse if you have any bruising or bleeding. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if you have any uncontrolled bleeding.**
Constipation	• You may have bowel motions (stools, poo) that are less frequent, harder, smaller, painful or difficult to pass. • You may also get: ◦ bloating, cramping or pain ◦ a loss of appetite ◦ nausea or vomiting. • Drink plenty of fluids (unless you are fluid restricted). • Eat plenty of fibre-containing foods such as fruit, vegetables and bran. • Take laxatives as directed by your doctor. • Try some gentle exercise daily. • **Tell your doctor or nurse if you have not opened your bowels for more than 3 days.**
Dizziness or feeling light-headed (orthostatic hypotension)	• You may get low blood pressure from the drug thalidomide. • You may feel dizzy or light-headed . • Tell your doctor if you are taking blood pressure medication. • Your doctor will monitor your blood pressure regularly while you are on this treatment. • When you want to get up from a sitting or lying down position, get up slowly to let your body adjust to the new position. • Tell your doctor or nurse if you get any of the signs or symptoms listed above.

Feeling sleepy or drowsy	• You may feel sleepy or drowsy. • This is caused by the drug thalidomide. • These symptoms will usually get better with time. • Take your thalidomide at night, so that you are not drowsy during the day. • Do not drive or operate machinery if you are feeling sleepy or drowsy.
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.**
Nausea and vomiting	• You may feel sick (nausea) or be sick (vomit). • Take your anti-sickness medication as directed even if you don't feel sick. • 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. • 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.**
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.**
Nerve damage (peripheral neuropathy)	• You may notice a change in the sensations in your hands and feet, including: ◦ tingling or pins and needles ◦ numbness or loss of feeling ◦ pain. • You may find it difficult to do everyday activities, such as doing up buttons or picking up small objects. • Test water temperature with your elbow when bathing to avoid burns. • Use rubber gloves, pot holders and oven mitts in the kitchen. • Wear rubber shoes or boots when working in the garden or garage. • Keep rooms well lit and uncluttered. • Ask your doctor or nurse for eviQ patient information – Nerve problems during cancer treatment. • Tell your doctor or nurse if you get any of the symptoms listed above.

Side effects from steroid medication	• Steroid medication may cause:
	  ◦ mood swings and behaviour changes
	  ◦ an increased appetite
	  ◦ weight gain
	  ◦ swelling in your hands and feet
	  ◦ stomach upsets
	  ◦ trouble sleeping
	  ◦ fragile skin and bruising
	  ◦ an increase in your blood sugar level
	  ◦ weak and brittle bones (osteoporosis)
	• Take your steroid medication with food to reduce stomach upset
	• If you have diabetes, your blood sugar levels may be tested more often.
	• Tell your doctor or nurse if you get any of the symptoms listed above.

Skin rash	• You may get a red, bumpy rash and dry, itchy skin. • Moisturise your skin with a gentle non-perfumed moisturising cream like sorbolene or aqueous cream. • Do not scratch your skin. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and sunscreen of SPF 50 or higher. • **Talk to your doctor or nurse about other ways to manage your skin rash.**

Blood clots (thromboembolism)	• Blood clots can occur with this 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:**
	  ◦ **redness, heat or pain in your leg(s)**
	  ◦ **numbness or weakness in your face, arm or leg**
	  ◦ **chest pain**
	  ◦ **sudden shortness of breath**
	  ◦ **dizziness**
	  ◦ **trouble speaking**
	  ◦ **blurred vision**
	  ◦ **severe headache**
	  ◦ **unexplained falls or loss of balance.**

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 loss (alopecia)	• Your hair may start to fall out from your head and body. • Hair loss usually starts 2 to 3 weeks after your first treatment. • You may become completely bald and your scalp might feel tender. • Use a gentle shampoo and a soft brush. • Take care with hair products like hairspray, hair dye, bleaches and perms. • Protect your scalp from the cold with a hat, scarf or wig. • Protect your scalp from the sun with a hat or sunscreen of SPF 50 or higher. • Moisturise your scalp to prevent itching. • Ask your doctor or nurse about the Look Good Feel Better program

Delayed (onset months to years)	
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.**
Lung problems	• Lung problems are rare, but can be serious. They may occur throughout treatment or after the completion of treatment. • You may get: ◦ shortness of breath ◦ fever ◦ dry cough ◦ wheezing ◦ fast heartbeat ◦ chest pain. • Your doctor will monitor how well your lungs are working during your treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have chest pain or become short of breath.**

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 and food safety

- 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.
- You should not drink alcohol while you are taking thalidomide, as it may increase the drowsiness and sleepiness caused by thalidomide.
- If you have any concerns about recent weight loss or weight gain or questions about your diet, ask to speak to a dietitian.
- There are some foods that may cause infection in high risk individuals and should be avoided. For further information on foods to avoid and food hygiene please ask for a copy of the Listeria and food brochure.

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

- This treatment can cause major congenital disabilities or death 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. You must use contraception while having this treatment and after stopping treatment, see the "Important information" section above for more information. 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.

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

Where to get more information

Telephone support

- Call Cancer Council on 13 11 20 for cancer information and support
- Call the Leukaemia Foundation on 1800 620 420 (Mon to Fri 9am – 5pm)
- Call the Lymphoma Nurse Support Line on 1800 953 081 (Mon to Fri 9am - 5pm)

Haematology, transplant and cellular therapy information

- Arrow bone marrow transplant foundation – arrow.org.au
- Australasian Menopause Society – menopause.org.au
- Chris O'Brien Lifehouse - Total Body Irradiation - mylifehouse.org.au/departments/radiation-oncology/total-body-irradiation/
- Healthy Male Andrology Australia – healthymale.org.au/
- International Myeloma Foundation – myeloma.org

- Leukaemia Foundation – leukaemia.org.au
- Lymphoma Australia – lymphoma.org.au
- Myeloma Australia – myeloma.org.au
- NSW Agency for Clinical Innovation, Blood & Marrow Transplant Network – aci.health.nsw.gov.au/resources/blood-and-marrow-transplant
- NSW Agency for Clinical Innovation - aci.health.nsw.gov.au/projects/immune-effector-cell-service
- NCCN Guidelines for Patients Immunotherapy Side Effects: CAR T-Cell Therapy - nccn.org/patientresources/patient-resources/guidelines-for-patients
- Talk Blood Cancer – cmlsupport.org.uk/organisation-type/social-media-groups

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
- eviQ Cancer Treatments Online – eviQ.org.au
- Food Standards Australia New Zealand: Listeria & Food Safety – foodstandards.gov.au/publications/pages/listeriabrochuretext.aspx
- 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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