Multiple myeloma LCD (lenalidomide CYCLOPHOSPHamide dexamethasone) SUPERSEDED

ID: 1394 v.6 **Superseded** Essential Medicine List

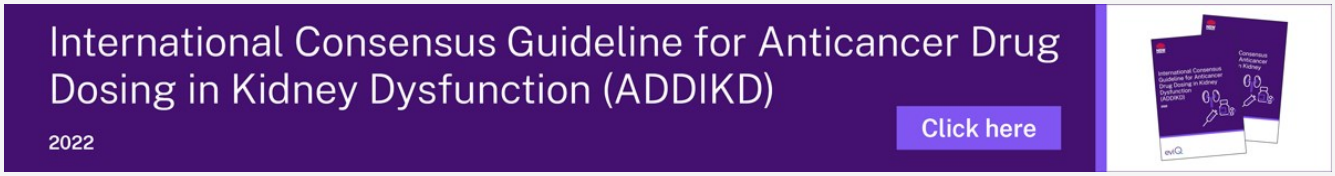
This protocol has been superseded as this therapy does not provide any additional benefit over lenalidomide and dexamethasone alone and is not commonly used upfront in clinical practice. Cyclophosphamide may be added if a clinical response is not obtained. ID 547 Lenalidomide and dexamethasone is the preferred regimen.

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 to 9

Drug	Dose	Route	Day
Dexamethasone	40 mg ONCE a week	PO	1, 8, 15, 22
CYCLOPHOSPHamide	300 mg/m^2 ONCE a week	PO	1, 8, 15, 22
Lenalidomide	25 mg ONCE a day	PO	1 to 21

Frequency: 28 days

Cycles: 9 maximum

Notes:

It is the consensus of the Haematology Reference Committee that:

- Dexamethasone 40 mg is given weekly as per the Rajkumar et al. trial[1] and clinical practice, and that cyclophosphamide be given at a dose of 300 mg/m^2 weekly.
- A 20 mg/week starting dose of dexamethasone should be considered in patients > 75 years.[2]

Drug status: **Cyclophosphamide** and **dexamethasone**: PBS general schedule

Lenalidomide: TGA registered for this indication but not PBS reimbursed in this combination.

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

Full prescribing information and Authority Application forms available from the Department of Human Services website

Lenalidomide is available as **5 mg**, **10 mg, 15 mg** and **25 mg** capsules

Cyclophosphamide is available as **50 mg** tablets

Dexamethasone is available as **4 mg** and **0.5 mg** tablets

Cost: ~ $2,550 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 to 9

Day 1		
Granisetron	2 mg (PO)	60 minutes before chemotherapy
Dexamethasone	40 mg (PO)	ONCE a week on days 1, 8, 15 and 22. Take in the morning with food.
CYCLOPHOSPHamide	300 mg/m^2 (PO)	ONCE a week on days 1, 8, 15 and 22. Take in the morning.
Lenalidomide	25 mg (PO)	ONCE a day on days 1 to 21. Take at same time each day, either with or without food.

Day 2 to 7		
Lenalidomide	25 mg (PO)	ONCE a day on days 1 to 21. Take at same time each day, either with or without food.

Day 8		
Granisetron	2 mg (PO)	60 minutes before chemotherapy
Dexamethasone	40 mg (PO)	ONCE a week on days 1, 8, 15 and 22. Take in the morning with food.
CYCLOPHOSPHamide	300 mg/m^2 (PO)	ONCE a week on days 1, 8, 15 and 22. Take in the morning.
Lenalidomide	25 mg (PO)	ONCE a day on days 1 to 21. Take at same time each day, either with or without food.

Day 9 to 14		
Lenalidomide	25 mg (PO)	ONCE a day on days 1 to 21. Take at same time each day, either with or without food.

Day 15		
Granisetron	2 mg (PO)	60 minutes before chemotherapy
Dexamethasone	40 mg (PO)	ONCE a week on days 1, 8, 15 and 22. Take in the morning with food.
CYCLOPHOSPHamide	300 mg/m^2 (PO)	ONCE a week on days 1, 8, 15 and 22. Take in the morning.
Lenalidomide	25 mg (PO)	ONCE a day on days 1 to 21. Take at same time each day, either with or without food.

Day 16 to 21		
Lenalidomide	25 mg (PO)	ONCE a day on days 1 to 21. Take at same time each

Day 16 to 21		
		day, either with or without food.

Day 22		
Granisetron	2 mg (PO)	60 minutes before chemotherapy
Dexamethasone	40 mg (PO)	ONCE a week on days 1, 8, 15 and 22. Take in the morning with food.
CYCLOPHOSPHamide	300 mg/m^2 (PO)	ONCE a week on days 1, 8, 15 and 22. Take in the morning.

Note: It is the consensus of the Haematology Reference Committee that dexamethasone 40 mg is given weekly as per the Rajkumar et al. trial[1] and clinical practice, and that cyclophosphamide be given at a dose of 300 mg/m^2 weekly. Dexamethasone may be reduced to 20 mg/week in patients > 75 years, BMI < 18.5, with poorly controlled diabetes mellitus or prior intolerance to steroid therapy.

Frequency: 28 days

Cycles: 9 maximum

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
Emetogenicity MODERATE	Suggested default antiemetics have been added to the treatment schedule, and may be substituted to reflect institutional policy. As a steroid has been included as part of this protocol, additional antiemetic steroids are not required. For patients with a prior episode of chemotherapy induced nausea or vomiting, a NK1 receptor antagonist may be available on the PBS in combination with a 5HT$_3$ antagonist and steroid. Ensure that patients also have sufficient antiemetics for breakthrough emesis: Metoclopramide 10 mg three times a day when necessary (maximum of 30 mg/24 hours, up to 5 days) OR Prochlorperazine 10 mg PO every 6 hours when necessary. Read more about preventing anti-cancer therapy induced nausea and vomiting

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
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
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).[3] 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
Antiviral prophylaxis	Read more about antiviral prophylaxis drugs and doses

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, LFTs, LDH and BSL baseline then 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).

Initial treatment with lenalidomide should not be started if ANC is less than 1.0 x 10^9/L and/or platelets less than 75 x 10^9/L (or platelets less than 30 x 10^9/L if heavy bone marrow involvement), however, may be commenced at the discretion of the treating haematologist.

Dose reduction steps for lenalidomide to manage haematological toxicities	
Starting dose	25 mg
Dose level 1	15 mg
Dose level 2	10 mg
Dose level 3	5 mg

Haematological toxicity	
ANC x 10^9/L (pre-treatment blood test)	
First fall to less than 0.5	Interrupt lenalidomide treatment

Haematological toxicity	
Return to greater than or equal to 0.5 when neutropenia is only observed toxicity	Resume lenalidomide at starting dose
Return to greater than or equal to 0.5 when dose-dependant haematological toxicities other than neutropenia are observed	Resume lenalidomide at dose level 1
For each subsequent drop less than 0.5	Interrupt lenalidomide treatment
Return to greater than or equal to 0.5	Resume lenalidomide at next lower dose level (dose level 2 or 3) Do not dose below 5 mg
Consider using G-CSF for neutropenia	
Platelets x 10^9/L (pre-treatment blood test)	
First fall to less than 30	Interrupt lenalidomide treatment
Return to greater than or equal to 30	Resume lenalidomide at dose level 1
For each subsequent drop less than 30	Interrupt lenalidomide treatment
Return to greater than or equal to 30	Resume lenalidomide at next lower dose level (dose level 2 or 3) Do not dose below 5 mg

Renal impairment	
Lenalidomide	
Lenalidomide is substantially excreted by the kidneys. Monitoring of renal function is advised in all patients with renal impairment. The following dose adjustments are recommended at the ***start of therapy*** for patients with moderate or severe impaired renal function or end stage renal disease.	
Creatinine clearance (mL/min)	
30 to 50	Reduce lenalidomide dose to 10 mg once daily *
less than 30 (not requiring dialysis)	Reduce lenalidomide dose to 15 mg on alternate days (every 48 hours)
less than 30 (requiring dialysis)	Reduce lenalidomide dose to 5 mg once daily. On dialysis days, administer the dose following dialysis

** The dose may be escalated to 15 mg after 2 cycles if the patient is not responding to treatment and is tolerating treatment.*

Cyclophosphamide	
Creatinine clearance (mL/min)	
less than 20 *	Reduce cyclophosphamide by 25%

** It is the consensus of the reference committee to adopt the cyclophosphamide dose modification reported by Kropff et al.[4] per the trial exclusion criteria, in the CyBorD (cyclophosphamide, bortezomib and dexamethasone) protocol due to similar patient populations.*

Hepatic impairment
No formal studies of lenalidomide in patients with hepatic impairment, therefore no specific dose recommendations.

Dermatological reaction[5, 6]	
Rare cases of Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported. These may be potentially fatal.	
Rash	
Grade 1	Continue lenalidomide. Treat with topical corticosteroids and oral antihistamines.
Grade 2	Consider interruption of lenalidomide. Treat with topical corticosteroids and oral antihistamines until toxicity resolves.

Dermatological reaction[5, 6]	
Grade 3	Consider interruption of lenalidomide. Treat with oral antihistamines or oral corticosteroids until toxicity resolves.
Stevens-Johnson syndrome or toxic epidermal necrolysis	Permanent discontinuation of lenalidomide treatment.

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*

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

Lenalidomide		
	Interaction	**Clinical management**
Digoxin	Potentially increased digoxin plasma levels when combined with lenalidomide; mechanism unknown	Monitor digoxin levels and for signs of drug toxicity during treatment with lenalidomide
HMG-CoA reductase inhibitors (Statins)	Potentially additive toxicity	Monitor for signs and symptoms of myotoxicity and rhabdomyolysis (e.g.: unexplained muscle pain, muscle stiffness or tenderness, dark urine) during concomitant use
Erythropoietic agents, combined oral contraceptives or hormone replacement therapy	Additive risk of thromboembolic events due to an increased risk of VTE	Consider the benefit/risk of concomitant therapy

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

This is an oral treatment

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

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

Peripheral neuropathy assessment tool.

Any toxicity grade 1 or greater may require dose reduction or delay of treatment and review by medical officer before commencing treatment.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Dexamethasone

- administer orally ONCE a week in the morning on **days 1, 8, 15 and 22** every 28 days
- to be taken with or immediately after food.

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

Chemotherapy - Time out

Cyclophosphamide

- administer orally ONCE a week in the morning on **days 1, 8, 15 and 22** every 28 days
- to be swallowed whole with a glass of water; do not break, crush or chew
- patients should be well hydrated and be encouraged to void frequently during treatment to prevent cyclophosphamide induced bladder irritation.

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

Lenalidomide

- administer orally ONCE a day, at the same time each day, on **days 1 to 21** every 28 days
- to be swallowed whole with a glass of water; do not break, crush or chew
- can be taken either with or without food

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

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

Days 2 to 7

This is an oral treatment

Safe handling and waste management (reproductive risk only)

Safe administration

General patient assessment prior to each day of treatment.

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

Peripheral neuropathy assessment tool.

Any toxicity grade 1 or greater may require dose reduction or delay of treatment and review by medical officer before commencing treatment.

Treatment - Time out

Lenalidomide

- administer orally ONCE a day, at the same time each day, on **days 1 to 21** every 28 days
- to be swallowed whole with a glass of water; do not break, crush or chew
- can be taken either with or without 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).

Day 8

This is an oral treatment

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

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

Peripheral neuropathy assessment tool.

Any toxicity grade 1 or greater may require dose reduction or delay of treatment and review by medical officer before commencing treatment.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Dexamethasone

- administer orally ONCE a week in the morning on **days 1, 8, 15 and 22** every 28 days
- to be taken with or immediately after food.

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

Chemotherapy - Time out

Cyclophosphamide

- administer orally ONCE a week in the morning on **days 1, 8, 15 and 22** every 28 days
- to be swallowed whole with a glass of water; do not break, crush or chew
- patients should be well hydrated and be encouraged to void frequently during treatment to prevent cyclophosphamide induced bladder irritation.

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

Lenalidomide

- administer orally ONCE a day, at the same time each day, on **days 1 to 21** every 28 days
- to be swallowed whole with a glass of water; do not break, crush or chew
- can be taken either with or without food

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

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

Days 9 to 14

This is an oral treatment

Safe handling and waste management (reproductive risk only)

Safe administration

General patient assessment prior to each day of treatment.

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

Peripheral neuropathy assessment tool.

Any toxicity grade 1 or greater may require dose reduction or delay of treatment and review by medical officer before commencing treatment.

Treatment - Time out

Lenalidomide

- administer orally ONCE a day, at the same time each day, on **days 1 to 21** every 28 days
- to be swallowed whole with a glass of water; do not break, crush or chew
- can be taken either with or without 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).

Day 15

This is an oral treatment

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

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

Peripheral neuropathy assessment tool.

Any toxicity grade 1 or greater may require dose reduction or delay of treatment and review by medical officer before commencing treatment.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Dexamethasone

- administer orally ONCE a week in the morning on **days 1, 8, 15 and 22** every 28 days
- to be taken with or immediately after food.

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

Chemotherapy - Time out

Cyclophosphamide

- administer orally ONCE a week in the morning on **days 1, 8, 15 and 22** every 28 days
- to be swallowed whole with a glass of water; do not break, crush or chew
- patients should be well hydrated and be encouraged to void frequently during treatment to prevent cyclophosphamide induced bladder irritation.

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

Lenalidomide

- administer orally ONCE a day, at the same time each day, on **days 1 to 21** every 28 days
- to be swallowed whole with a glass of water; do not break, crush or chew
- can be taken either with or without food

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

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

Days 16 to 21

This is an oral treatment

Safe handling and waste management (reproductive risk only)

Safe administration

General patient assessment prior to each day of treatment.

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

Peripheral neuropathy assessment tool.

Any toxicity grade 1 or greater may require dose reduction or delay of treatment and review by medical officer before commencing treatment.

Treatment - Time out

Lenalidomide

- administer orally ONCE a day, at the same time each day, on **days 1 to 21** every 28 days
- to be swallowed whole with a glass of water; do not break, crush or chew
- can be taken either with or without 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).

Day 22

This is an oral treatment

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

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

Peripheral neuropathy assessment tool.

Any toxicity grade 1 or greater may require dose reduction or delay of treatment and review by medical officer before commencing treatment.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Dexamethasone

- administer orally ONCE a week in the morning on **days 1, 8, 15 and 22** every 28 days
- to be taken with or immediately after food.

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

Chemotherapy - Time out

Cyclophosphamide

- administer orally ONCE a week in the morning on **days 1, 8, 15 and 22** every 28 days
- to be swallowed whole with a glass of water; do not break, crush or chew
- patients should be well hydrated and be encouraged to void frequently during treatment to prevent cyclophosphamide induced bladder irritation.

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

Lenalidomide

- administer orally ONCE a day, at the same time each day, on **days 1 to 21** every 28 days
- to be swallowed whole with a glass of water; do not break, crush or chew
- can be taken either with or without food

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

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

Discharge information

Dexamethasone, cyclophosphamide tablets and lenalidomide capsules

- Dexamethasone, cyclophosphamide tablets and lenalidomide capsules with written instructions on how to take them.

Antiemetics

- Antiemetics as prescribed.

Thromboprophylaxis

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

Growth factor support

- Arrangements for administration if prescribed.

Prophylaxis medications

- Prophylaxis medications (if prescribed) i.e. tumour lysis prophylaxis, PJP prophylaxis, antifungals, 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)	
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting
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
Thrombocytopenia	A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding. Read more about thrombocytopenia
Anorexia	Loss of appetite accompanied by decreased food intake. Read more about anorexia
Arthralgia and myalgia	Generalised joint pain or and/or stiffness and muscle aches, often worse upon waking or after long periods of inactivity. Can improve with movement. May be mild or severe, intermittent or constant and accompanied by inflammation. Read more about arthralgia and myalgia
Constipation	
Cough	
Diarrhoea	Read more about treatment induced diarrhoea
Fatigue	Read more about fatigue
Haemorrhagic cystitis	An inflammatory process, characterised by diffuse mucosal inflammation with haemorrhage involving the entire bladder. Patients are at risk following treatment with cyclophosphamide, ifosfamide and radiation therapy. Read more about haemorrhagic cystitis
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
Respiratory tract infection	
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
Diarrhoea (late onset)	Chronic loose stools due to bile acid malabsorption has been observed in patients receiving lenalidomide. Referral to Gastroenterology should be considered. An empiric trial of cholestyramine (a bile-acid binding resin) is reasonable for these patients. Read more about treatment induced diarrhoea
Hypothyroidism	
Muscle cramps	Cramping in the hands, calves and/or thighs associated with hypomagnesaemia (low magnesium) and/or hypocalcaemia (low calcium).
Stevens-Johnson syndrome (SJS)	Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN) is characterised by fever, malaise, a painful rash, erythematous macules, targetoid lesions, or diffuse erythema progressing to vesicles and bullae, and oral, ocular and/or genital mucositis with painful mucosal erosion. Patients who develop SJS/TEN should never be re-exposed to the causative agent.

Delayed (onset months to years)	
Cataract	A disorder characterised by partial or complete opacity of the crystalline lens of one or both eyes. This results in a decrease in visual acuity and eventual blindness if untreated.
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

This protocol has been superseded as this therapy does not provide any additional benefit over lenalidomide and dexamethasone alone and is not commonly used upfront in clinical practice.

A search of the literature found limited evidence to support the use of LCD (Lenalidomide, cyclophosphamide, dexamethasone) in the treatment of relapsed refractory multiple myeloma (RRMM). The expert reference panel supported publication of the protocol on the basis of the information summarised below. While there are further data to support the combination of lenalidomide, cyclophosphamide and corticosteroid[7, 8] in MM, the committee was most strongly influenced by Schey et al.[9]

This was a phase 1/2 dose escalation study involving 31 patients with median 3 lines of previous therapy. The design of the study involved addition and escalation of cyclophosphamide in which 600 mg was the maximum tolerated dose, lenalidomide (25 mg D1 to 21) and dexamethasone (20 mg D1 to 4, D8 to 11) for a maximum of 9 cycles followed by single-agent lenalidomide.[9]

Contentious issues: small number of patients (i.e. 31) and dose-escalation design.

Source	Study & Year Published	Supports Use	Is the dose and regimen consistent with the protocol?	Comments
Phase II trials	Schey et al. 2010	**Yes**	No	Dexamethasone 20 mg D1 to 4 and 8 to 11, lenalidomide 25 mg D1 to 21, cyclophosphamide 600 mg D1 and 8 every 28 days
	Reece et al. 2015	**Yes**	Yes	Cyclophosphamide 300 mg/m^2 on D1, 8 and 15,

Source	Study & Year Published	Supports Use	Is the dose and regimen consistent with the protocol?	Comments
				lenalidomide 25 mg on D1 to 21 and prednisone 100 mg every other day in a 28 day cycle
Case series	Morgan et al. 2007	**Yes**	Yes	-
Observational studies	-	**N/A**	-	-
Guidelines	**Date published/revised**	**Supports Use**	**Is the dose and regimen consistent with the protocol?**	**Comments**
NCCN	V.4 2015	**Yes**	N/A	-
BCCA	-	**Yes**	-	-
MSAG	2012	**Yes**	no	Lenalidomide PO 25 mg D1 to 21, cyclophosphamide PO 500 mg weekly, dexamethasone PO 40 mg D1 to 4 and D12 to 15

Efficacy

Only 10/31 patients reached target cyclophosphamide dose of 700 mg, and approximately 50% of patients received dose-reduction of lenalidomide due to neutropenia. Of those responding, 90% had best response at cycle 6. Of those tolerating maximum dose (cyclophosphamide 700 mg), there was complete response (CR) in 4/10 and partial response (PR) in 6/10. Overall this study had 80% overall survival (OS) at 30 months and 56% progression-free survival (PFS) at 2 years. This was considered favourable by the Haematology Reference Committee. There was no difference in response based on high-risk cytogenetic abnormalities, $ß_2$microglobulin or tolerated cyclophosphamide dose.[9]

Toxicity

All patients commenced 25 mg lenalidomide, with dose reduction in ~50% by cycle 9. Overall, there was a 41% neutropenia rate, with 19% being grade 3 to 4.[9] Overall, the toxicity profile was manageable and did not differ considerably from published data for lenalidomide-dexamethasone.[10]

Table 3. Grade 3 and 4 Adverse Events.*

Event	Lenalidomide (N=176)		Placebo (N=175)	
	Grade 3	Grade 4	Grade 3	Grade 4
	number (percent)			
Hematologic disorder				
Neutropenia	44 (25.0)	8 (4.5)	4 (2.3)	0
Anemia	14 (8.0)	1 (0.6)	12 (6.9)	0
Thrombocytopenia	17 (9.7)	3 (1.7)	7 (4.0)	3 (1.7)
Febrile neutropenia	5 (2.8)	1 (0.6)	0	0
Gastrointestinal disorder				
Constipation	3 (1.7)	0	2 (1.1)	0
Diarrhea	5 (2.8)	0	4 (2.3)	0
Nausea	2 (1.1)	0	0	0
General disorder				
Asthenia	11 (6.2)	0	10 (5.7)	0
Fatigue	11 (6.2)	1 (0.6)	6 (3.4)	0
Pyrexia	1 (0.6)	0	6 (3.4)	0
Peripheral edema	2 (1.1)	0	3 (1.7)	0
Infection				
Upper respiratory infection	3 (1.7)	0	0	0
All other infection†	15 (8.5)	2 (1.1)	9 (5.1)	2 (1.1)
Weight loss	3 (1.7)	0	1 (0.6)	0
Musculoskeletal or connective-tissue disorder				
Muscle cramp	1 (0.6)	0	0	0
Back pain	4 (2.3)	0	3 (1.7)	0
Bone pain	5 (2.8)	0	3 (1.7)	0
Muscle weakness	13 (7.4)	0	8 (4.6)	0
Arthralgia	1 (0.6)	0	3 (1.7)	0
Neurologic disorder				
Headache	1 (0.6)	0	1 (0.6)	0
Tremor	2 (1.1)	0	2 (1.1)	0
Dizziness	1 (0.6)	0	1 (0.6)	0
Paresthesia	1 (0.6)	0	0	0
Insomnia	2 (1.1)	0	1 (0.6)	0
Respiratory, thoracic, or mediastinal disorder				
Cough	2 (1.1)	0	1 (0.6)	0
Nasopharyngitis	1 (0.6)	0	0	0
Dyspnea	4 (2.3)	1 (0.6)	2 (1.1)	1 (0.6)
Vascular disorder				
Deep-vein thrombosis	6 (3.4)	1 (0.6)	5 (2.9)	1 (0.6)
Pulmonary embolism	2 (1.1)	6 (3.4)	1 (0.6)	1 (0.6)
Venous thromboembolism‡	13 (7.4)	7 (4.0)	6 (3.5)	2 (1.1)

* Listed are data that were available on December 31, 2005. Percentages may not total 100 because of rounding.
† This condition was also described in the following terms: infections not otherwise specified, pneumonia, upper respiratory tract infection, upper respiratory viral infection, sepsis, bacterial infection, urinary tract infection, pharyngitis, nasopharyngitis, febrile neutropenia, oral candidiasis, oral fungal infection, primary atypical pneumonia, fungal sinusitis, herpes simplex, herpes zoster, herpes encephalitis, herpes viral infection, cytomegalovirus pneumonia, and viral infection.
‡ This condition was also described in the following terms: deep-vein thrombosis, pulmonary embolism, pulmonary infarction, thrombosis, phlebothrombosis, thrombophlebitis, superficial thrombophlebitis, venous thrombosis, thromboembolism, splenic-vein thrombosis, phlebitis, and superficial phlebitis.

References

1 Rajkumar, S. V., S. Jacobus, N. S. Callander, R. et al. 2010. "Lenalidomide plus high-dose dexamethasone versus lenalidomide plus low-dose dexamethasone as initial therapy for newly diagnosed multiple myeloma: an open-label randomised controlled trial." Lancet Oncol 11(1):29-37.

2 Quach, H., M. H. Prince and S. Harrison on behalf of MSAG. 2022. “Clinical practice guideline multiple myeloma.” Myeloma Foundation of Australia.

3 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.

4 Kropff, M., G. Bisping, E. Schuck, et al. 2007. "Bortezomib in combination with intermediate-dose dexamethasone and continuous low-dose oral cyclophosphamide for relapsed multiple myeloma." Br J Haematol 138(3):330-337.

5 Celgene Pty Ltd. Product Information REVLIMID® (lenalidomide) capsules. Date of First Approval 20 December 2007, Date of most recent amendment 03 March 2016

6 Tinsley, S. M., S. E. Kurtin and J. A. Ridgeway. 2015. "Practical Management of Lenalidomide-Related Rash." Clin Lymphoma

Myeloma Leuk 15 Suppl:S64-69.

7 Reece, D. E., E. Masih-Khan, E. G. Atenafu, et al. 2015. "Phase I-II trial of oral cyclophosphamide, prednisone and lenalidomide for the treatment of patients with relapsed and refractory multiple myeloma." Br J Haematol 168(1):46-54.

8 van de Donk, N. W., S. Wittebol, M. C. Minnema, et al. 2010. "Lenalidomide (Revlimid) combined with continuous oral cyclophosphamide (endoxan) and prednisone (REP) is effective in lenalidomide/dexamethasone-refractory myeloma." Br J Haematol 148(2):335-337.

9 Schey, S. A., G. J. Morgan, K. Ramasamy, et al. 2010. "The addition of cyclophosphamide to lenalidomide and dexamethasone in multiply relapsed/refractory myeloma patients; a phase I/II study." Br J Haematol 150(3):326-333.

10 Dimopoulos, M., A. Spencer, M. Attal, et al. 2007. "Lenalidomide plus dexamethasone for relapsed or refractory multiple myeloma." N Engl J Med 357(21):2123-2132.

Bibliography

Morgan, G. J., S. A. Schey, P. Wu, et al. 2007. "Lenalidomide (Revlimid), in combination with cyclophosphamide and dexamethasone (RCD), is an effective and tolerated regimen for myeloma patients." Br J Haematol 137(3):268-269.

History

Version 6

Date	Summary of changes
13/04/2023	This protocol has been updated with the following changes: • 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' • Lenalidomide administration details updated in treatment schedule, administration and patient information • Note regarding dexamethasone reduction in specific patient populations added to treatment schedule notes • Specific medications removed from G-CSF note in 'Dose modifications' section • Dose modifications for rash updated to align with product information • Cataract, cough, respiratory tract infection and diarrhoea (late onset) added to side effects Changed to Version 6.

Version 5

Date	Summary of changes
31/08/2012	New protocol taken to Haematology Reference Committee meeting.
21/08/2013	Approved and published on eviQ. Review in 2 years (category 2).
13/03/2015	Reviewed at the Haematology Reference Committee meeting. The following updates were made: • Title changed to LCD from RCD to reflect generic names. • Dexamethasone dose was changed to 40 mg weekly. Note added to explain consensus of the Haematology Reference Committee. Review in 2 years.
18/10/2015	Removed reference to 'i-Access™ Program'.
31/05/2017	Transferred to new eviQ website. Version number changed to v.3.
24/11/2017	Reviewed at the Haematology Reference Committee meeting: • Cyclophosphamide dose changed from 500 mg to 300 mg/m^2 to be in line with other oral cyclophosphamide-containing myeloma protocols on eviQ as per reference committee consensus decision. Updated the note under the treatment schedule to reflect this.

Date	Summary of changes
	• Reference to the 'i-Access™ program' added back into drug status. • Version number changed to v.4. • Next review in 2 years.
24/05/2019	Reviewed at the Haematology Reference Committee meeting: • Protocol superseded as protocol would rarely be used upfront with ID 547 Lenalidomide and dexamethasone considered as standard therapy. • Version number changed to v.5 • Next review in 2 years.
10/10/2019	Clinical information updated with PBS expanded indications for G-CSF.
29/11/2021 **20/01/2022**	Interactions updated.
24/01/2022	Pulmonary toxicity added to side effects.

First approved: 8 August 2013
Last reviewed: 24 May 2019
Review due: 31 December 2021
Superseded: 14 June 2019

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/1394
09 Jun 2023

Patient information - Multiple myeloma - LCD (lenalidomide, cyclophosphamide, dexamethasone)

Patient's name:

Your treatment

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

LCD (lenalidomide, cyclophosphamide, dexamethasone)		
This treatment cycle is repeated every 28 days. You will have up to 9 cycles.		
Day	**Treatment**	**How it is given**
1, 8, 15 and 22	**Dexamethasone** *(dex-a-METH-a-sone)*	Take orally ONCE a week in the morning with food on days 1, 8, 15 and 22 only.
	Cyclophosphamide *(SYE-kloe-FOS-fa-mide)*	Take orally ONCE a week in the morning on days 1, 8, 15 and 22 only. Swallow whole, do not break, crush or chew tablets.
1 to 21	**Lenalidomide** *(LEN-a-LID-oh-mide)*	Take orally ONCE a day on days 1 to 21 only at the same time every day. Take either with or without 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.
- **Cyclophosphamide**: if you forget to take your tablets or vomit your tablets, take your normal dose the next time it is due. Do not take an extra dose.
- **Lenalidomide**: if you forget to take a capsule and if it less than 12 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 • 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:

Important information about taking lenalidomide

Lenalidomide 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.

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

- **If you are a male patient and your female partner is of child-bearing potential** you **must** use a barrier method of contraception (e.g. condoms) while taking lenalidomide and for one week after finishing lenalidomide 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 lenalidomide. You should start using contraception four weeks before taking lenalidomide and continue for four weeks after finishing lenalidomide treatment. It is important that you discuss appropriate contraception with your doctor.

If you become pregnant while taking lenalidomide you must stop the treatment and tell your doctor immediately. If you are a male patient and your female partner becomes pregnant 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

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

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.
- **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.

Superseded treatments

This treatment is superseded meaning that better treatments have taken its place. Uncommonly superseded treatments are still used. Your doctor will explain why this treatment has been selected for you.

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)	
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.**
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.**

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.**
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.
Joint and muscle pain and stiffness	• You may get muscle, joint or general body pain and stiffness. • Applying a heat pack to affected areas may help. • Talk to your doctor or nurse about other ways to manage these symptoms. You may need medication to help with any pain.

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.**

Cough	• Some people who receive this treatment develop a cough • Tell your doctor or nurse if you develop a cough
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.**

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.**
Bladder irritation (haemorrhagic cystitis)	• You may get: ◦ blood in your urine, sometimes with blood clots ◦ pain or burning when you urinate ◦ the urge to urinate more than normal ◦ stomach or pelvic pain or discomfort. • When you go home, make sure you drink plenty of fluids (unless you are fluid restricted). • Empty your bladder often. • **Tell your doctor or nurse as soon as possible if you notice any blood in your urine.**
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.
Chest infection	• You can develop a chest infection whilst receiving this treatment. • **Tell your doctor or nurse as soon as possible if you get any of the following symptoms:** ◦ **shortness of breath** ◦ **difficulty breathing** ◦ **wheezing** ◦ **coughing up mucus**
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
Diarrhoea (late onset)	• Whilst usually mild and easily manageable, bowel motions (stools, poo) that are more frequent or more liquid may persist during treatment with lenalidomide. • Bile acid malabsorption (BAM), a condition in which patients do not absorb bile acids properly from their intestines, can be a cause of persistent diarrhoea in patients taking lenalidomide. • It can be treated by making some dietary changes such as making sure that fat does not make up more than 20% of the diet. • Your doctor will recommend if treatment is necessary for your diarrhoea • Drink plenty of fluids (unless you are fluid restricted). • 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.**
Slow thyroid gland (hypothyroidism)	• You may: ◦ fatigue and low energy levels ◦ depression ◦ slow heart rate ◦ unexplained weight gain ◦ intolerance to cold temperatures ◦ fatigued and aching muscles ◦ dry, coarse skin ◦ puffy face ◦ hair loss ◦ constipation ◦ problems with concentration • You will have regular blood tests to check how well your thyroid is working • **Tell your doctor or nurse if you get any of the symptoms listed above.**
Muscle cramps	• You may get muscle cramps, usually in the hands, calves and thighs. • Tell your doctor or nurse if you get any of these symptoms. Your doctor may prescribe you medication for this.
Stevens-Johnson syndrome (SJS)	• This side effect is rare, but can be very serious. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following symptoms:** ◦ **flu-like symptoms, then a painful red or purple rash that spreads** ◦ **swelling of the face or tongue** ◦ **painful or peeling skin** ◦ **blisters on the skin, mouth, nose, eyes and genitals.**

Delayed (onset months to years)	
Cataract	• Tell your doctor or nurse if you notice any changes to your eyes, including blurred vision.
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.
- 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.
- 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

Additional notes:

First approved: 8 August 2013
Last reviewed: 24 May 2019
Review due: 31 December 2021
Superseded: 14 June 2019

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/1394
09 Jun 2023