Multiple myeloma MPT (melphalan prednisolone thalidomide) oral SUPERSEDED

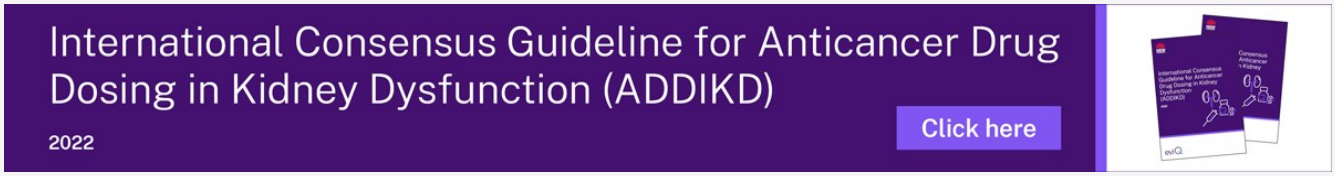
ID: 61 v.4 **Superseded** Essential Medicine List

This protocol has been superseded due to the availability of second and third generation IMiDs.

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

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 12

Drug	Dose	Route	Day
Prednisolone	2 mg/kg ONCE a day	PO	1 to 4
Melphalan	0.2 mg/kg ONCE a day	PO	1 to 4
Thalidomide	100 mg ONCE a day	PO	1 to 42

Frequency: 42 days

Cycles: 12

Notes:

- Melphalan has erratic absorption, if no myelosuppression occurs after oral dosing, poor oral absorption should be suspected.
- Administer with caution within 4 weeks of radiation therapy.

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

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

Melphalan and **prednisolone:** PBS general schedule

Melphalan is available as **2 mg** tablets
Thalidomide is available as **50 mg** and **100 mg** capsules
Prednisolone is available as **25 mg**, **5 mg** and **1 mg** tablets

Cost: ~ $920 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 12

Day 1 to 4		
Prednisolone	2 mg/kg (PO)	ONCE a day on days 1 to 4. Take in the morning with food.
Melphalan	0.2 mg/kg (PO)	ONCE a day on days 1 to 4. Take on an empty stomach, at least half an hour before, or two hours after food.
Thalidomide	100 mg (PO)	ONCE a day continuously. Take in the evening at least one hour after food.
Day 5 to 42		
Thalidomide	100 mg (PO)	ONCE a day continuously. Take in the evening at least one hour after food.

Frequency: 42 days

Cycles: 12

Indications and patient population

- Upfront treatment of previously untreated 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 minimal or low	No routine prophylaxis required. If patients experience nausea and/or vomiting, consider using the low emetogenic risk regimen. 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

Administration details	Thalidomide should be taken at least one hour after food in the evening to minimise daytime drowsiness. Melphalan should be taken on an empty stomach, at least half an hour before, or 2 hours after food. Melphalan tablets should be stored in the fridge (2 to 8 degrees C). Prednisolone should be taken in the morning with food.
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).[1] 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
Blood tests	FBC, EUC, LFTs, LDH and BSL at baseline, prior to each cycle and regularly throughout treatment 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	
Neutrophils less than 1.0 x 10^9/L and/or platelets less than 75 x 10^9/L	Delay melphalan until recovery unless due to marrow infiltration and consider dose reduction on subsequent cycles

Myelosuppression from melphalan is cumulative from which recovery can be prolonged or incomplete

Renal impairment	
Creatinine clearance (mL/min)	
30 to 50	Reduce melphalan by 25%
less than 30	Clinical decision but not recommended

Hepatic impairment
No specific dose modifications recommended for melphalan. If excessive toxicity, consider dose reduction on subsequent cycles.

Peripheral sensory neuropathy	
Grade 2	Withhold thalidomide until peripheral neuropathy resolves to grade 1, then reinstate at

Peripheral sensory neuropathy	
	50% dose reduction. If sensory neuropathy is associated with neuropathic pain, cease thalidomide.[2]
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*

Melphalan (oral)		
	Interaction	**Clinical management**
Ciclosporin	Additive nephrotoxicity	Monitor renal function and ciclosporin levels: dose reduction of ciclosporin may be necessary when used with high dose melphalan

Prednisolone		
	Interaction	**Clinical management**
Antidiabetic agents (e.g. insulin, glibenclamide, glicazide, metformin, pioglitazone, etc)	The efficacy of antidiabetic agents may be decreased	Use with caution and monitor blood glucose
Azole antifungals (e.g. fluconazole, itraconazole, ketoconazole, posaconazole)	Increased toxicity of prednisolone possible due to reduced clearance	Avoid combination or monitor for prednisolone toxicity
Oestrogens (e.g. oral contraceptives)	Increased toxicity of prednisolone possible due to reduced clearance	Avoid combination or monitor for prednisolone toxicity. Dose reduction of prednisolone may be required
Ritonavir	Increased toxicity of prednisolone possible due to reduced clearance	Avoid combination or monitor for prednisolone toxicity

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

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

Administer antiemetics if required

Note: melphalan and prednisolone is given only on days 1 to 4 every 42 days, and thalidomide is given each day continuously every 42 days.

Prednisolone

- administer orally ONCE a day on **days 1 to 4**
- in the morning with or after food

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

Chemotherapy - Time out

Melphalan

- administer orally ONCE a day
- to be swallowed whole with a glass of water; do not break, crush or chew
- to be taken on an empty stomach, one hour before or two hours after food
- store tablets in the fridge (2 to 8 degrees C).

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

Thalidomide

- administer orally ONCE a day in the evening
- 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 until 7 days after completion of drug(s)

Days 5 to 42

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.

Note: melphalan and prednisolone is given only on days 1 to 4 every 42 days, and thalidomide is given each day continuously every 42 days.

Treatment - Time out

Thalidomide

- administer orally ONCE a day in the evening
- 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

Melphalan and prednisolone tablets and thalidomide capsules

- Melphalan and prednisolone tablets and thalidomide 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.

Laxatives

- Ensure patient has prophylactic laxatives.

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)	
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting
Headache	

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
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 - partial	Hair thinning and/or patchy hair loss. Patients can also experience mild to moderate discomfort of the hair follicles, and rarely pain as the hair is falling out. Read more about alopecia and scalp cooling

Evidence

This protocol has been superseded due to the availability of second and third generation IMiDs.

In a multicentre study by Palumbo et al.,[3, 4, 5] 255 patients with newly diagnosed multiple myeloma were randomised to receive either standard melphalan and prednisolone (MP) or melphalan, prednisolone plus thalidomide (MPT). 126 patients received MP and 129 received MPT at the doses used in this regimen. 50% of the patients enrolled were aged >72 years, with half of these aged >75years. This study concluded that MPT was more effective with respect to response rate (RR), progression-free survival (PFS) and possibly survival, than MP, particularly when in patients >65 years and in younger patients ineligible for stem cell transplantation (SCT). These results need to be balanced against the increased toxicities associated with MPT, although the

upfront use of thromboprophylaxis can reduce some of the toxicities.

In the IFM99-06 study, Facon et al.[6] randomised 447 patients with de novo myeloma, aged 65-75 years, to receive either MP (n=196), MPT (n=125) or reduced intensity SCT using melphalan 100 mg/m^2 (n = 126). The dose of thalidomide used in this trial was higher than in the Palumbo studies, with a dose of up to 400 mg/day and the number of cycles of MP was also increased (12 cycles). Findings were consistent with Palumbo et al., with MPT demonstrating superior RR, PFS and overall survival than the other arms of the study. The authors concluded that MPT should be the standard treatment for newly diagnosed elderly patients with multiple myeloma and others who are not eligible for SCT albeit with a reduced dose of thalidomide and upfront thromboprophylaxis.

The French IFM 01/01 study by Hulin et al.[7] further consolidated the efficacy and tolerability of MPT in elderly patients with myeloma. A total of 229 patients over the age of 75 were randomised to either MPT or MP. All patients received melphalan (0.2 mg/kg/d) plus prednisone (2 mg/kg/d) for 12 courses (day 1 to 4) every 6 weeks. Patients were randomly assigned to receive 100 mg/d of oral thalidomide (n = 113) or placebo (n = 116), continuously for 72 weeks. The primary end point for the trial was overall survival.

Efficacy

In both the Palumbo and Facon studies, outcomes were statistically significantly superior for MPT over MP.

In Palumbo (2006), median time to attain a partial response was 1.4 months (range 22-200 days) for MPT and 3.1 months (25-210 days) for MP.[4] Median follow up from diagnosis was 38.4 months (0.23 to 69.4 months) for MPT and 37.7 months (0 to 72.3 months) for MP. The PFS was 21.8 months for MPT and 14.5 months for MP (P=0.004). Median overall survival (OS) was 45.0 months for MPT and 47.6 months for MP (P =0.79). Complete response rates for MPT was 15.6% compared to 3.7% for MP (P<0.001).[5]

Overall median follow up for the Facon study was 51.5 months (34.4 to 63.2 months),[6] while the Hulin study had a median follow up of 47.5 months.[7]

Results for the two French trials are summarised in the table below:

Outcome	IFM 99-06 (Facon et al.)[6] 65-75 years of age		IFM 01/01 (Hulin et al.)[7] over 75 years of age	
	MP n = 191	MPT n = 125	MP n = 112	MPT n = 107
CR %	2	15	1	7
ORR%	40	81	39	90
PFS, months	17.8	27.5	18.5	24.1
OS	38.3 months (13.8 - 54.8)	51.6 months (26.6 - not reached)	29.1 months (26.4 - 34.9)	44.0 months (33.4 - 58.7)

Toxicity

Overall, Grade 3 or 4 adverse events occurred in 62 (49%) patients receiving MPT and 32 (25%) of those treated with MP.[6] The most common of these are summarised in the table below.

11 deaths (8%) adverse event-related deaths were reported in the MPT arm (cardiac failure (2), ventricular fibrillation (1), ventricular tachycardia (1), AMI (1), pneumonia (4), PUO (1) and thromboembolism (1)). 6 adverse event-related deaths were reported in the MP arm (cardiac failure (3), ventricular tachycardia (1) and pneumonia (1).

In the 65 patients who received MPT prior to the implementation of thromboprophylaxis, 37 experienced grade 3-4 adverse events, including 11 with thromboembolism. In those who received thromboprophylaxis (64), grade 3-4 adverse events occurred in 25 patients - only 2 developed thromboembolism.

The development of ≥ grade 2 peripheral neuropathy resulted in thalidomide dose reduction to 50 mg in 12 patients after a median of 5.8 months.[6] In the IFM99-06 trial, 45% patients discontinued thalidomide because of toxic effects, mainly peripheral neuropathy, between 3 and 16 months.[4]
The incidence and range of grade 3 to 4 adverse events was similar in the Facon et al study.[6]

Adverse Events[4] Grade 3-4	MPT Number (%) (n=129)	MP Number (%) (n=126)
Neutropenia	21 (16)	22 (17)
Thrombocytopenia	4 (3)	5 (4)
Anaemia	4 (3)	5 (4)
DVT	12 (9)	2 (2)
PE	3 (2)	0 (0)
Peripheral Neuropathy	10 (8)	0 (0)
Somnolence/fatigue	3 (3)	1 (1)
Cardiac failure	4 (3)	4 (3)
Constipation	8 (6)	0 (0)
Rash	3 (2)	0 (0)
Pneumonia	6 (5)	2 (2)
PUO	3 (2)	0 (0)

References

1 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.

2 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.

3 Palumbo, A., A. Bertola, P. Musto, et al. 2005. "Oral melphalan, prednisone, and thalidomide for newly diagnosed patients with myeloma." Cancer. 104(7):1428-1433.

4 Palumbo, A., S. Bringhen, T. Caravita, et al. 2006. "Oral melphalan and prednisone chemotherapy plus thalidomide compared with melphalan and prednisone ....." Lancet. 367(9513):825-831.

5 Palumbo, A., S. Bringhen, A. M. Liberati, et al. 2008. "Oral melphalan, prednisone, and thalidomide in elderly patients with multiple myeloma: updated results of a randomized controlled trial." Blood 112(8):3107-3114.

6 Facon, T., J. Y. Mary, C. Hulin, et al. 2007. "Melphalan and prednisone plus thalidomide versus melphalan and prednisone alone or reduced-intensity autologous stem cell transplantation....." Lancet. 370(9594):1209-1218.

7 Hulin, C., T. Facon, P. Rodon, et al. 2009. "Efficacy of melphalan and prednisone plus thalidomide in patients older than 75 years with newly diagnosed multiple myeloma: IFM 01/01 trial." J Clin Oncol 27(22):3664-3670

History

Version 4

Date	Summary of changes
30/04/2021	Protocol reviewed at Haematology Reference Committee meeting. Consensus decision to supersede protocol due to the availability of second and third generation IMiDs. Version number changed to v.4. For review in 2 years.
21/12/2021	Changed antiemetic clinical information block to minimal or low, to align with new categories. See ID 7 Prevention

Date	Summary of changes
	of anti-cancer therapy induced nausea and vomiting (AINV) v5.
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" section, 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'

Version 3

Date	Summary of changes
09/05/2007	Minor editing and reformatting
04/07/2007	Addition of information and minor editing
07/09/2009	Reviewed and transferred to eviQ
15/01/2010	Updated 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
06/12/2011	New format to allow for export of protocol information. Protocol version number changed to v.2. Antiemetics and premedications added to the treatment schedule. Additional Clinical Information, Key Prescribing table and Key Administration table combined into new section titled Clinical Considerations. Drug specific information placed behind the drug name link.
20/01/2012	PHC view added.
30/03/2012	Thalidomide has been reclassified from minimal to low emetic potential to align with MASCC Antiemetic Guideline 2011.
31/08/2012	Protocol reviewed using the stratified review process at the Haematology Reference Committee meeting. No change and next review in 2 years.
19/06/2013	Added new bisphosphonate and VTE clinical information block.
13/03/2015	Change to treatment schedule, dose and days of prednisolone and melphalan changed. New evidence from the french IFM 01/01 study added.
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	Protocol reviewed using the stratified review process at the Haematology Reference Committee meeting. Reference to the 'i-access™ program' added back into drug status. Dose modification updated as per Delforge et al 2010 paper. No significant changes, review again in 5 years.

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https://www.eviq.org.au/p/61
09 Jun 2023

Patient information - Multiple myeloma - MPT (melphalan, prednisolone, thalidomide)

Patient's name:

Your treatment

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

MPT (melphalan, prenisolone, thalidomide)		
This treatment cycle is repeated every 42 days. You will have 12 cycles.		
Day	**Treatment**	**How it is given**
1 to 4	**Prednisolone** (*pred-NIS-oh-lone*)	Take orally ONCE a day in the morning with food on days 1 to 4 only.
	Melphalan *(MEL-fa-lan)*	Take orally ONCE a day in the morning on days 1 to 4 only. Take on an empty stomach, at least one hour before or two hours after food. Swallow tablets whole, do not break, chew or crush. Melphalan tablets need to be stored in the fridge.
1 to 42	**Thalidomide** *(tha-LID-oh-mide)*	Take orally ONCE a day in the evening on days 1 to 42. Take on an empty stomach at least one hour after eating a meal. Swallow capsules whole, do not break, open, chew or crush.

Missed doses:

- **Melphalan** and **prednisolone**: 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 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 38°C or higher • chills, sweats, shivers or shakes • shortness of breath • uncontrolled vomiting or diarrhoea • pain, tingling or discomfort in your chest or arms • you become unwell.	Daytime: Night/weekend: Other instructions:

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

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

Other medications given during this treatment

- **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.

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.**
Headache	• You can take paracetamol if you have a headache. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get a very bad headache that is not helped by pain medication.**

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.**

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 thinning	• Your hair may become dry and may break easily. • You may lose some of your hair. • Use a gentle shampoo and a soft hairbrush. • Take care with hair products like hairspray, hair dye, bleaches and perms. • Protect your scalp from the cold with a hat or scarf. • Protect your scalp from the sun with a hat and sunscreen of SPF 50 or higher. • Ask your doctor or nurse about the Look Good Feel Better program (www.lgfb.org.au)

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.
- 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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