SACT PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

MPT
MELPHALAN, PREDNISOLONE &THALIDOMIDE
MYELOMA

PROTOCOL REF: MPHAMPTMPT
(Version No. 1.0)

Approved for use in:

- First line treatment of myeloma in patients who are ineligible for high dose chemotherapy with a stem cell transplant.
- Relapsed multiple myeloma in patients who are ineligible for stem cell transplant.

Dosage:

Drug	Dose	Route	Frequency
Melphalan	**7mg/m^2**	PO	Daily on Days 1 to 4 of cycle
Prednisolone	***40mg/m^2**	PO	Daily on Days 1 to 4 of cycle
Thalidomide	****50mg**	PO	Once daily at night continuously

*Dose of prednisolone can be reduced at clinician discretion
**Titrate dose of thalidomide up to 200mg daily

Cycle length every 28 to 42 days. Continue until plateau phase (paraprotein level stable for 3 months) up to a maximum of 9 cycles and then stop.

Administration (+/- Counselling Points):

- The prescriber must inform male and female patients about the expected teratogenic risk and the strict pregnancy prevention measures as specified in the pregnancy prevention program and provide patients with appropriate patient educational brochure and patient card

- A thalidomide treatment initiation form (TIF) must be completed prior to initiation of thalidomide and prescription authorisation form (PAF) must be completed prior to each thalidomide prescription as detailed in the BMS pregnancy prevention program.
- VTE prophylaxis is required throughout treatment due to thrombotic effect of thalidomide.
- Thalidomide should be taken as a single dose at bedtime, to reduce the impact of somnolence. Capsules should not be opened or crushed.
- Prednisolone tablets should be taken in the morning after food.

Pregnancy Prevention Programme (PPP):

Due to the increased risk of birth defects associated fetal exposure to thalidomide the following should be adhered to:

- A Treatment Initiation Form (TIF) must be completed prior to treatment initiation (cycle 1) with thalidomide
- A Prescription Authorisation Form (PAF) must be completed by the prescriber for each supply of thalidomide. This must be approved by a pharmacist when verifying each prescription and confirmation of dispensing completed by the relevant dispensing pharmacy. Supply must be completed within 7 days of the prescription generation.
- A maximum of 3 months can be supplied for men or women of non-child bearing potential
- A maximum of 1 month can be supplied for women of child bearing potential. A negative pregnancy test must be confirmed within 3 days of prescription generation.

Emetogenic risk:

Mildly emetogenic.

Supportive treatments:

- Allopurinol oral 300mg once daily (first cycle only)
- Aciclovir oral 400mg twice daily
- Co-trimoxazole oral 480mg once daily
- Chlorhexidine 0.2% mouthwash 10ml twice a day
- Metoclopramide oral 10mg three times daily when required

- Nystatin oral suspension 1mL four times daily or fluconazole 50mg PO once daily (higher risk patients only)
- Omeprazole 20mg once daily
- VTE prophylaxis:
    - Dalteparin 5,000 units subcutaneous injection daily (or alternative prophylactic low molecular weight heparin (LMWH))
    - Therapeutic dose LMWH in high risk patients. Patients may continue previously established DOAC treatment or be switched to a LMWH.
    - Aspirin oral 75mg daily (for those patients who decline LMWHs or for those deemed to be low risk on long term treatment)

Dosing in renal and hepatic impairment:

Renal		
Melphalan	GFR: 30 – 50 mL/min	75% dose
	GFR: < 30mL/min	Clinical decision
Thalidomide	Thalidomide has not formally been studied in patients with impaired renal function. No specific dose recommendations for these patient populations are available. Patients with severe organ impairment should be carefully monitored for adverse reactions.	

Hepatic	
Melphalan	No recommendations, if excess toxicity reduce dose for subsequent cycles
Thalidomide	Thalidomide has not formally been studied in patients with impaired renal or hepatic function. No specific dose recommendations for these patient populations are available. Patients with severe organ impairment should be carefully monitored for adverse reactions.

Interactions:

Melphalan: No interactions of note with low dose oral melphalan.

Thalidomide:

- Thalidomide has sedative properties, thus may enhance the sedation induced by anxiolytics, hypnotics, antipsychotics, H1 antihistamines, opiate derivatives, barbiturates

and alcohol. Caution should be used when thalidomide is given in combination with medicinal products that cause drowsiness.

- Due to thalidomide's potential to induce bradycardia, caution should be exercised with medicinal products having the same pharmacodynamic effect such as active substances known to induce torsade de pointes, beta blockers or anticholinesterase agents.
- Combined oral contraceptives are not recommended due to the increased risk of venous thromboembolic disease.

For more detailed interactions please refer to the SPC

Main toxicities:

Thalidomide
Thrombocytopenia, neutropenia, anaemia, nausea, vomiting, diarrhoea, drowsiness, venous thromboembolism, peripheral neuropathy, injection site reactions, infusion related reactions, high blood sugars, teratogenicity
Melphalan
Anaemia, thrombocytopenia, neutropenia, nausea, vomiting, diarrhea, temporary significant elevation of the blood urea has been seen in the early stages of melphalan therapy in myeloma patients with renal damage

Investigations and treatment plan:

	Pre-initiation	Each cycle	Ongoing
Informed Consent	x		
Clinical Assessment	x	x	Continue post treatment as indicated
SACT Assessment (to include PS and toxicities)	x	x	Every cycle
FBC, U&E & LFTs, bone profile	x	x	Every cycle
CrCl (Cockcroft and Gault)	x	x	Every cycle
Paraprotein, immunoglobulins, serum free light chains, beta 2 microglobulin, electrophoresis and immunofixation.	x	x	Every cycle (can be extended in stable patients at clinician discretion)
Virology screening (Hep B, Hep C, HIV)	x		
HbA1C	x		Repeat as clinically indicated
Blood glucose	x		If clinically indicated
Pregnancy test			As clinically indicated
Thalidomide prescription authorization form	x	x	With every prescription
Neurological assessment (for neuropathy)	x	x	Every cycle
Weight recorded	x	x	Every cycle
Height recorded	x		
Imaging as per NICE/network guidance and clinical indication	x		To restage as indicated

Dose Modifications and Toxicity Management:

Haematological toxicity:

Proceed on day of treatment if:

ANC >1.0 x 10^9/L	Platelets >75 x 10^9/L

If cytopenias are thought to be disease related then treatment may go ahead at clinician discretion.

Consider the following dose reductions for neutropenia / thrombocytopenia:

Haematological parameter			Dose reduction
ANC <1.0 x 10^9/L	Or	Platelets <50 x 10^9/L	Consider dose reduction
If prolonged ANC <0.5 x 10^9/L	Or	If prolonged platelets <25 x 10^9/L with bleeding	Reduce melphalan to 75% original dose

These haematological guidelines assume that patients are well with stable performance status, that other acute toxicities have resolved.

Non - Haematological toxicity:

See Section entitled Dosing in Renal and Hepatic Impairment.

Peripheral Neuropathy (thalidomide)

Severity of neuropathy	Modification of dose and regimen
Grade 1 (paraesthesia, weakness and/or loss of reflexes) with no loss of function	Consider reducing dose if symptoms worsen. Dose reduction is not necessarily followed by improvement of symptoms.
Grade 2 (interfering with function but not with activities of daily living)	Reduce dose / interrupt treatment and continue to monitor. Discontinue if no improvement or continued worsening of the neuropathy. If the neuropathy resolves to Grade 1 or better, the treatment may be restarted.
Grade 3 (interfering with activities of daily living) or Grade 4 (disabling neuropathy)	Discontinue treatment

References:

1. Summary of Product Characteristics, Melphalan 2mg tablets, Aspen. March 2014. Monograph available from: http://www.medicines.org.uk
2. Summary of Product Characteristics, Thalidomide 50mg BMS. Sept 2023. Monograph available from: http://www.medicines.org.uk
3. Bortezomib and thalidomide for the first line treatment of multiple myeloma. NICE TA228. Published July 2011.
4. Krens S D, Lassche, Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. Lancet Oncol 2019; 20: e201–08

Circulation/Dissemination

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Version History

Date	Version	Author name and designation	Summary of main changes
Oct 2023	1.0	**Jennifer Gibson Principal Pharmacist HO**	**New Protocol**