MPT

A first-line option for myeloma patients in whom high dose therapy is not planned.
May also be used in relapsed patients.

Drugs/Dosage:

Melphalan		$4mg/m^2$ po once daily for 7 days (Day 1 to Day 7)
Prednisolone		$40mg/m^2$ po once daily for 7 days (Day 1 to Day 7)
+/-		
Thalidomide		initial dose 50mg po once daily, titrating upwards after 2 weeks to a maximum of 100mg once daily, continuous throughout treatment, depending on tolerability

Other Drugs:

Allopurinol according to renal function – review after 4 weeks
Omeprazole 20mg od (or ranitidine) is recommended whilst treating with steroids
Fluconazole 100mg po od as antifungal prophylaxis
plus, if thalidomide prescribed;
Laxative as required for thalidomide-induced constipation
Thromboprophylaxis, according to unit practice, is recommended in the absence of specific contraindication

Administration:

Melphalan available as 2mg tablets, which need to be stored in the fridge.
Prednisolone, available as 5mg, 20mg and 25mg tablets, are to be taken in the morning with or after food.
Thalidomide is available as 50mg capsules. The daily dose should be taken at bedtime to avoid problems with day-time sedation. Patients should be advised not to drive or operate machinery for 8 hours after each dose.

Frequency: every 4 weeks for 6 cycles

Main Toxicities:

myelosuppression; teratogenicity (see Comments); dry skin or rash;
sedation (take thalidomide at bedtime); peripheral neuropathy;
constipation (often requiring laxatives); dizziness; bradycardia and syncope;
increased risk of thromboembolic events; steroid side effects; ovarian failure; infertility

Anti-emetics: mildly emetogenic

Regular Investigations:

FBC	before each cycle, and as indicated
U&Es & LFTs	before each cycle
Paraprotein and/or serum free light chains	every 4 - 8 weeks
Pregnancy test	every 4 weeks for women of child bearing potential

Comments:

Thalidomide is highly teratogenic.
Women of child bearing potential must have a negative pregnancy test within 3 days prior to starting treatment. Pregnancy testing should be repeated monthly thereafter until one month after stopping thalidomide (or every 2 weeks in women with irregular menstrual cycles). If a woman taking thalidomide thinks she may be pregnant she must stop the drug immediately.

Men taking thalidomide must use a barrier method of contraception throughout treatment and for one week after stopping, if their partner is capable of bearing children.

Reason for Update: fluconazole added; general review	Approved by Chair of Alliance TSSG: Dr A Laurie
Version: 4	Date: 6.2.17
Supersedes: Version 3	Review date: Feb 2020
Prepared by: S Taylor	Checked by: C Tucker

Women of child-bearing potential must use one agreed effective method of contraception for at least 4 weeks before starting thalidomide, while on thalidomide and for one month after. (The combined oral contraceptive pill is not recommended due to the increased risk of thromboembolism)

Thalidomide is supplied through the Celgene Pregnancy Prevention Programme.
All aspects of the programme should be followed, including completion of an authorisation form by both doctor and pharmacist with every cycle.

Dose Modifications

Haematological Toxicity: If neutrophils < 1.0 x 10^9/L or platelets < 75 x 10^9/L, treatment should be deferred unless low counts are thought to be due to myeloma per se.
If severe myelotoxicity occurs, consider either a dose reduction or changing to cyclophosphamide

Renal Impairment: Suggested dosing for non-transplant patients[1]:

CrCl (ml/min)	Melphalan dosing
>50	Give 100% dose
10 - 50	Give 75% dose
<10	Give 50% dose

Thalidomide Side Effects: Mild neuropathy is very common and, in the absence of progression of the neuropathy, the thalidomide dose may be kept the same. If the symptoms begin to worsen, consider a dose reduction of up to 50%.
For Grade 2 neuropathy, a dose reduction of up to 50%, or a break in treatment, is required. If neuropathy does not improve, discontinue thalidomide permanently. If neuropathy resolves to Grade 1 or better, continue with the 50% dose if risk/benefit favourable.
In more severe cases (Grade 3 – 4), it is recommended that thalidomide should be permanently discontinued. However, if symptoms do resolve, re-introducing thalidomide at a lower dose may be considered. However, neuropathy is often not reversible.

Patient Information: Macmillan Leaflet for MPT
Celgene Pregnancy Prevention Programme Booklet

References:
Palumbo, A et al; Lancet 2006; 367: 825 – 831
[1]UCLH Dosage adjustment guidelines for Cytotoxics in Renal Impairment, 2009

Reason for Update: fluconazole added; general review	Approved by Chair of Alliance TSSG: Dr A Laurie
Version: 4	Date: 6.2.17
Supersedes: Version 3	Review date: Feb 2020
Prepared by: S Taylor	Checked by: C Tucker