SACT PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

CYCLOPHOSPHAMIDE (ORAL) WEEKLY MYELOMA

PROTOCOL REF: MPHACYMYHA
(Version No. 1.1)

Approved for use in:

Myeloma patients who are frail and unsuitable for immunomodulatory or protease inhibitor therapy.

Blueteq registration is not required.

Dosage:

Drug	Dose	Route	Frequency
Cyclophosphamide	**500mg**	PO	Days 1, 8, 15 and 22
Dexamethasone	**10mg**	PO	Days 1, 8, 15 and 22 **NB the dexamethasone can be omitted**

Cycle length every 28 days. Continue until plateau, disease progression or unacceptable toxicity.

Administration / counselling:

- Cyclophosphamide should be taken on an empty stomach; that is an hour before food or two hours after food.
- Dexamethasone should be taken in the morning after food

Emetogenic risk:

Moderately emetogenic

Supportive treatments:

- Allopurinol 300mg daily oral (reduce dose if the patient has renal dysfunction) for the first cycle
- Aciclovir PO 400mg twice daily if on steroids
- Co-trimoxazole PO 480mg daily if on steroids
- Omeprazole PO 20mg once daily (if dexamethasone is prescribed)
- Metoclopramide PO 10mg three times daily when required

Dosing in renal and hepatic impairment:

Renal Dose Modifications		
	Creatinine Clearance (mL/min)	**Dose Modification**
Cyclophosphamide	10 – 29	Consider 75% dose
	<10	Not recommended. If unavoidable consider 50% of dose.

Hepatic Dose Modifications	
Cyclophosphamide	Not recommended in severe impairment

Interactions:

Substances that reduce the efficacy of cyclophosphamide include: aprepitant, bupropion, busulfan, ciprofloxacin, chloramphenicol, azole-antimycotics (e.g., fluconazole and itraconazole, CYP2B6 and CYP3A4 inhibitors (e.g. nevirapin and ritonavir). Co-administration may reduce the efficacy of cyclophosphamide, prasugrel, sulphonamides, e.g. sulfadiazine, sulfamethoxazole and sulfapyridine, thiotepa, grapefruit (fruit or juice), rifampicin, St. John's wort.

<u>An increased risk of side-effects may occur with:</u>

Azathioprine: (increased risk of hepatotoxicity (liver necrosis)), chloral hydrate, cimetidine, disulfiram, glyceraldehyde, protease inhibitors, saquinavir, rifampin, phenobarbital, carbamazepine, phenytoin, St. John's wort, benzodiazepines, corticosteroids and dabrafenib.

There is an increased risk of cardiotoxicity when cyclophosphamide is co-administered with: anthracyclines, mitomycin, cytarabine, pentostatin and radiation therapy.

Please refer to the SPC for full list of interactions and further information.

Treatment schedule:

Day	Drug	Dose	Route	Diluent and rate
1	**Cyclophosphamide**	**500mg OD**	**PO**	Take on an empty stomach
	Dexamethasone	**10mg OD**	**PO**	In the morning with food
8	**Cyclophosphamide**	**500mg OD**	**PO**	Take on an empty stomach
	Dexamethasone	**10mg OD**	**PO**	In the morning with food
15	**Cyclophosphamide**	**500mg OD**	**PO**	Take on an empty stomach
	Dexamethasone	**10mg OD**	**PO**	In the morning with food
22	**Cyclophosphamide**	**500mg OD**	**PO**	Take on an empty stomach
	Dexamethasone	**10mg OD**	**PO**	In the morning with food

Main toxicities:

Cyclophosphamide
Myelosuppression, anaemia, neutropenia, thrombocytopenia, infection, haemolytic uraemic syndrome, abnormal hepatic function, alopecia, cystitis, micro-haematuria, hemorrhagic cystitis, fever, mucosal inflammation,

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 2	Cycle 3+	Ongoing
Informed consent	X				
Clinical Assessment	X	X	X	X	
SACT Assessment (including performance status and toxicity assessment)		X	X	X	
FBC	X	X	X	X	
U&E & LFTs & Calcium profile	X	X	X	X	
CrCl (Cockcroft and Gault)	X				
Serum Igs/electrophoresis/serum free light chains (if indicated)	X	X	X	X	
Dental assessment	X				
HbA1C and blood glucose	X				Repeat as clinically indicated
Imaging as per NICE/network guidance and clinical indication	X				Repeat as clinically indicated
Height	X				
Weight	X	X	X	X	Every cycle
Pregnancy test	X				If clinically indicated

Dose Modifications and Toxicity Management:

Haematological toxicity:

Proceed on day 1 if-

ANC ≥ 1.0 x 10^9/L	Platelets ≥ 50 x 10^9/L

If the patient has persistent cytopenias, which are not thought to be disease related, omitting cyclophosphamide for 1 to 3 weeks, reducing cyclophosphamide dose or adding G-CSF can be tried.

These haematological guidelines assume that patients are well with good performance status, that other acute toxicities have resolved and the patient has not had a previous episode of neutropenic sepsis.

Non- Haematological toxicity:

See section 'Dose modifications for Renal and Hepatic Impairment'

References:

1. Summary of Product Characteristics, Cyclophosphamide tablets 50mg. Updated Dec 2016. Accessed 29th June 2023.
2. 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

Date added into Q-Pulse	For completion by DCM
Date document posted on the Intranet	For completion by DCM

Version History

		Author name and designation	Summary of main changes
June 2020	1.0	**Aileen McCaughey – HO Pharmacist**	**New protocol**
Aug 2023	1.1	**Jennifer Gibson – Principal HO Pharmacist**	**Three yearly review. New template. Updated indications.**