CARFILZOMIB & DEXAMETHASONE

Carfilzomib in combination with dexamethasone is recommended as an option for treating multiple myeloma in adults, only if they have only had 1 previous therapy and that did not include bortezomib
(induction chemotherapy followed by stem cell transplant is considered to be one line of therapy)

Blueteq registration is required before treatment may start

Drugs/Dosage:	**Carfilzomib**	20mg/m^2 (max 44mg)	IV	Day 1 and Day 2 of Cycle 1
		then, if tolerated, 56mg/m^2 (max 123mg)	IV	Day 8, 9, 15 & 16 of Cycle 1, and on Day 1, 2, 8, 9, 15 & 16 of subsequent cycles
	Dexamethasone	20mg	po	Day 1, 2, 8, 9, 15, 16, 22 and 23

Administration: **Carfilzomib** given by intravenous infusion in 100ml 5% glucose over 30 minutes.
To reduce the risk of tumour lysis, patient should be encouraged to drink 2 – 3 litres per day for the 2 days before day 1 of cycle 1
plus
250 - 500ml of sodium chloride 0.9% to be administered **before** each dose in cycle 1, followed by an additional 250 - 500ml of intravenous fluids **following** each carfilzomib administration in cycle 1

Monitor patient for evidence of volume overload - the total volume of fluid may be reduced as clinically indicated in patients with baseline cardiac failure or who are at risk for cardiac failure.

Oral and/or intravenous hydration should be continued, as needed, in subsequent cycles.

Dexamethasone is to be taken in the morning with or after food; and should be taken at least 30 minutes to 4 hours before any carfilzomib.

Other Drugs: Allopurinol, dose according to renal function – review after 3 weeks.
Consider PCP prophylaxis – prescribe according to unit practice/protocol.
Fluconazole 100mg po od as antifungal prophylaxis
Aciclovir 400mg po bd
Omeprazole 20mg od (or ranitidine) is recommended whilst treating with steroids.
Thromboprophylaxis should be considered, based on an assessment of the patient's underlying risks and clinical status

Frequency: Every 28 days
Treatment may be continued until disease progression or until unacceptable toxicity

Main Toxicities: myelosuppression; increased risk of infections; diarrhoea; dyspnoea; peripheral oedema; cardiac toxicity; pulmonary toxicities; hypertension; acute renal failure; hepatic toxicity; PRES; thrombotic microangiopathy; tumour lysis syndrome; infusion related reactions; steroid side effects

Anti- emetics: moderately emetogenic (but anti-emetic doses of dexamethasone not required)
Extravasation: carfilzomib is a non-vesicant

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Regular Investigations:	FBC	Day 1
	U&Es	Day 1
	LFTs	Day 1
	MUGA/echo	only if concerned
	Paraprotein and/or serum free light chains	every 4 weeks
	Blood glucose and blood pressure	tailored according to individual patient needs, while on high dose dexamethasone

Dose Modifications If a dose reduction with carfilzomib is required, the recommended steps are:
56mg/m^2 reduced to 45 mg/m^2; 45mg/m^2 reduced to 36mg/m^2; 36mg/m^2 reduced to 27mg/m^2

Haematological Toxicity:

FBC	Management
Neutrophils < 0.5 x 10^9/l or febrile neutropenia	Delay carfilzomib treatment. Once counts have recovered to ≥ 0.5 x 10^9/l and any fever has resolved, resume treatment at the same dose level. For subsequent drops to < 0.5 x 10^9/l, consider a carfilzomib dose reduction, as above, when re-starting.
Platelets < 10 x 10^9/l or evidence of bleeding with thrombocytopenia	Delay carfilzomib treatment. Once counts have recovered to ≥ 10 x 10^9/l and any bleeding controlled, resume treatment at the same dose level. For subsequent drops to < 10 x 10^9/l, consider a carfilzomib dose reduction, as above, when re-starting.

Renal Toxicity:	Serum creatinine ≥ 2 x baseline or CrCl < 15ml/min, or ≤ 50% of baseline or Need for dialysis	Delay carfilzomib. Re-start treatment when renal function has recovered to within 25% of baseline; and consider resuming carfilzomib at 1 dose level reduction.

Other non-haem Toxicity: For any other Grade 3 or 4 toxicity non-haematological toxicity, stop carfilzomib until resolved and then consider re-starting carfilzomib at 1 dose level reduction.

Renal Impairment: No starting dose adjustment for carfilzomib is recommended in patients with baseline mild, moderate, or severe renal impairment, or for patients on chronic dialysis.
For patients on dialysis, carfilzomib should be given after the dialysis procedure.

For renal impairment occurring after treatment has started, see above.

Hepatic Impairment: The pharmacokinetics of carfilzomib have not been evaluated in patients with severe hepatic impairment.
No starting dose adjustment is recommended in patients with mild or moderate hepatic impairment.

Patient Information: No Macmillan or CRUK leaflet currently available

References: Dimopoulos, M et al ; Lancet Oncology 2016 ; 17 (1) : 27 - 38

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